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CONTENTS.

On Tuberculosis as an Endemic Disease. Inaugural Address of Session 1892-93. By JOSEPH FRANK PAYNE, M.D., F.R.C.P., *President* - 1

Measles Epidemics, Major and Minor. By B. ARTHUR WHITELEGGE, M.D., County Medical Officer, West Riding, Yorkshire - - 37

Epidemic Dropsy. By KENNETH McLEOD, M.D., LL.D. - - 55

Post-Scarlatinal Diphtheria: a Statistical and Etiological Study. By R. D. R. SWEETING, B.A.(Oxon.), M.B.(Dublin), D.P.H.(Camb.), etc., *Hon. Treasurer of the Society* - - - - 94

On African Hæmoglobinuric Fever. By PATRICK MANSON, M.D., M.R.C.P., LL.D. - - - - - 111

Variola and Vaccinia: their Manifestations and Inter-relations in the Lower Animals. An Experimental Research. By S. MONCKTON COPEMAN, M.A., M.D.(Cantab.), Lecturer on Public Health, Westminster Hospital Medical School - - - - 142

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1867. Marshall, John, 13, Liverpool Street, Dover.
1860. May, George, jun., 43, Castle Street, Reading, Berks.
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TRANSACTIONS
OF
The Epidemiological Society of London.

INAUGURAL ADDRESS OF SESSION 1892–93.

On Tuberculosis as an Endemic Disease.

By JOSEPH FRANK PAYNE, M D, F.R.C.P., President.

(*Read: November 16th*, 1892.)

Gentlemen,—In taking the chair of this distinguished Society, I must commence by thanking you for the honour you have done me in electing me to this office, and expressing my sense of the great responsibility of following the numerous eminent men who have preceded me in this chair.

I have felt some difficulty in selecting any topic for my remarks to-night, which I could hope to present in a manner at all worthy of your hearing; but I hope that the subject of tubercular disease will not be regarded as foreign to the aim and scope of this Society. Our aim, as I find it defined in earlier addresses from this chair, has always been the investigation of the origin, propagation, mitigation, and treatment of epidemic diseases. The word epidemic has not, however, been understood to exclude the consideration of diseases which are rather endemic than epidemic; that is, looked at in relation to their distribution in space, rather than to their distribution in time. Moreover, phthisis, or tubercular disease in general, has been recently made the subject of several papers read before the Society, and we may assume that the study of this disease is now, whatever it may have been formerly, regarded as coming within the scope of the science of Epidemiology, taken in a wide sense.

If we enquire into the presumable reasons for this inclusion of tubercular disease in our province, we must, I think, assign it partly to a change which has recently taken place in our manner of regarding this disease.

The starting point of our modern conception of tubercle

was unconnected with and anterior to any doctrine of its being caused by a micro-organism. Villemin, in 1865, or earlier, had the happy thought of trying whether tubercular diseases could be conveyed by inoculation of tubercular products, like vaccinia and other inoculable diseases. His experiments gave, in the case of rodents, a positive result; and from that time, supposing Villemin's conclusions to be, as they were, confirmed by others, tubercular disease had to be transferred to the great class of specific diseases; that is, of those which are caused by some definite material virus, and not by various kinds of injuries, or by quantitative variations in the more general causes of disease, depending on nutrition, climate, and the like influences.

I need not recount the steps by which the undoubtedly serious objections brought against Villemin's theory by Wilson Fox, Burdon Sanderson, Cohnheim, and others were finally got rid of (as confessed by all these investigators themselves); till in 1881 Cohnheim was able clearly to formulate the theory that tubercle was due to a specific communicable cause, even though this cause was still unknown.

Even had this material cause never been actually discovered, the specific nature of tubercle would rest on the same footing as that of small-pox, scarlatina, and other exanthemata, with respect to which the same uncertainty as to the precise nature of the specific virus still remains.

Koch's brilliant discovery in 1882, identifying this unknown cause with a definite bacillus, came when the times were ripe.

The history of discovery in this subject has been the same as in the investigation of many obscure natural phenomena. The first step is to frame the hypothesis of a cause adequate to account for the phenomena: operating at the right time and in the right place. Further, it must be shown that no other cause is capable of producing the same effects, since it is not impossible *à priori* that the phenomena may be produced by more causes than one. But this will not be enough, since we can evidently invest a hypothetical cause with any properties we please. It must be shown that the supposed adequate cause really exists, and operates at the time and place supposed. The results of Villemin and his followers clearly showed what kind of cause was necessary to explain the occurrence of tubercle, and that no other of the causes assigned, such as inflammation, cachexia, etc., was adequate. It remained for Koch to show that such a cause, perfectly adequate to

explain the production of tubercle, actually existed, and was in operation at the time and place necessary to account for the phenomena of tubercular disease.

By these discoveries it has been clearly established that *tuberculosis* (and this modern name is in itself significant) belongs to the class of diseases with which the Epidemiological Society chiefly concerns itself.

It is true that tuberculosis differs from many of the diseases called specific in certain particulars—in its insidious onset and long duration, in having no self-determined limit of existence, and hence in not conferring (as is probable) any immunity against itself. Moreover, its mode of communication is obscure, and hence, some think, is not well expressed by the words infectious and contagious, which carry with them certain vague connotations. Nevertheless, it cannot be doubted that it is, in the strictest sense, communicable, for the inoculation of tubercle to animals is as certain as the inoculation, for instance, of vaccinia. Again, the prevalence of tuberculosis in man is much affected by external circumstances, by climate and conditions of soil, by density of population, by inherited constitution, and other influences. Still there is no one of these conditions which does not affect the prevalence and spread of some one or more of the diseases called specific. These facts do not at all disprove its causation by a definite material, living, and communicable virus, that is, by the bacillus of Koch, the only known cause which in any way accounts for its phenomena.

Endemic Existence of the Tubercular Disease.

The problem which I propose specially to consider is, what are the conditions which maintain the continued existence of tuberculosis as an endemic disease in any country or population? If the disease inevitably depends upon a certain organism, the tubercle bacillus, then the problem resolves itself into two: What are the conditions which maintain the continued existence of the tubercle bacillus? and, What are the conditions, if any, which would make the population proof against attack, *i.e.*, give immunity against the bacillus, even supposing it to be widely prevalent?

The second of these problems might be of great practical importance if the bacillus were regarded as ineradicable, or, at least, little affected by preventive measures. Whether its solution will ever be found we cannot say. I do not in

the least undervalue the importance of trying to find its solution. But, on the principle of one thing at a time, I shall not further refer to it, but confine myself to considering the causes of the prevalence or continued existence of the tubercle bacillus.

Continued Existence of the Tubercle Bacillus.

The continued existence of any living organism in any country will obviously depend upon its finding an appropriate habitat and abundant food, and also on the presence or absence of conditions militating against its existence.

As regards the tubercle bacillus, there is no doubt that its chief habitat is the human body, where it finds, as a parasite, its appropriate pabulum; and the conditions limiting its existence are only the conditions of health or the reverse which affect its vitality there. But it is also a very important question whether it can really live, that is, grow, outside the human body, in a saprophytic or ectogenic existence; or, again, whether it can at all events maintain its vitality, without growth, in such conditions, so as to be ready for development when introduced into the body again.

Koch, finding that he was unable to cultivate the bacillus except at temperatures between 82° and 105° F., and that the best temperature was 99.50° F.—that is, the temperature of internal parts of the human body—concluded that it was a true parasite, and incapable of growing in external nature, at all events in our climate. This conclusion is confirmed in the strongest manner by most bacteriologists. I find only one contrary observation, that of Sir Hugh Beevor, who, using the improved methods of cultivation introduced by M.M. Roux and Nocard, found that the bacillus would grow at the temperature of an ordinary room in winter, which was rarely above 60° F., and often much lower, though the growth below 99° F. was decidedly slow.*

These results seem to require confirmation, as I find they are not confirmed by the experience of most bacteriologists, but, if confirmed, they would show that the bacillus is capable of an ectogenic existence, and is not a true or obligatory parasite, but an occasional, or, as it is said, "facultative" one. Dr. Andrew and others support the same view on theoretical grounds. It is also evident that,

* *Trans. Path. Soc.*, London, 1891, vol. xlii, p. 344.

even according to Koch's conclusions, the temperature of air and soil in hot climates would not be unsuitable for the bacillus, provided sufficient moisture were present. On the other hand, all bacteriologists agree that the bacillus is extremely sensitive, or, so to speak, difficult to please in the matter of artificial cultivation-media, very few of the customary media suiting it, so that its artificial cultivation is one of the most difficult problems in practical bacteriology.

As regards its pabulum, it is found that moist albuminous materials, simple or peptonised, are the one essential constituent. Further, it has been found by Nocard and Roux that a product of the decomposition of fat, glycerine, accelerates the growth in a remarkable manner.*

It should be added that moisture, necessary to the growth of all bacteria, is preeminently so in the case of the tubercle bacillus, since the slightest drying of the surface of the cultivation-medium stops its growth, though without destroying its vitality. The bacillus is also aerobic, that is, needs a certain amount of oxygen for its growth. Now moist albuminous materials, mixed with products of fatty decomposition, are certainly present in or about the abodes of men and animals (though not in the open soil); and might conceivably, if at a proper temperature, form a suitable nidus for the growth of the bacillus. Nevertheless, we must conclude that the possibility of an ectogenic or non-parasitic growth of the bacillus is not certainly proved, and is, on the whole, in our climate, improbable. The question of such possibility in hot climates must remain for the present an open one. And it is worthy of note that a climate at once hot and moist seems, generally speaking, the most favourable for the spread of tubercular phthisis, as shown, for instance, by the higher mortality from phthisis in the British army in the West Indies than in Canada. Further, the belief in the contagiosity of phthisis (which would certainly be favoured by the conditions supposed) has always been most strongly held, and is so still, in comparatively hot countries such as southern Europe.

Independent of the possibility of growth and multiplication in external nature, there is an important possibility in the case of the bacillus, viz., whether it can maintain its *vitality* in conditions not admitting of actual growth, so as to be capable of growing again in more favourable circum-

* Nocard and Roux, *Annales de l'Institut Pasteur*, 1887, No 1, p. 19; Crookshank, *Trans. Path. Soc.*, 1891, vol. xlii, p. 330.

stances. Most bacteria, like other organisms, animal or vegetable, have the power of concentrating their vitality into special products, like seeds, capable of resisting adverse influences which would be fatal to the growing organisms. These products, viz., spores, are well known in many bacteria; but with regard to the tubercle bacillus there is considerable doubt as to whether the real spore has been found. The well-known beaded condition of the bacillus as seen in phthisical sputum is often spoken of as spore formation. But I must confess to an individual scepticism on this point. It is not proved that either the portions stained by ordinary reagents, or those unstained, are true spores. It is thought that the beaded or supposed spores containing bacilli are more resistant and tenacious of life. But, in fact, it is almost impossible to separate the apparently sporeless from the beaded forms, and Baumgarten has arrived at the conclusion that the difference in point of vitality observed between these forms in some species of bacteria does not hold in the case of the tubercle bacillus.*

However, spores or no spores, the bacilli have great powers of resistance to injurious influences—to dryness, to heat, to cold, to contact with putrefying substances, and to antiseptics. After being dried up for several months at ordinary temperatures they are still capable of growing and multiplying if introduced into an animal body, but several circumstances modify the possibility of revival. At a temperature of 86° to 104° the vitality declines much more rapidly than at ordinary air temperatures. But, in any case, after nine to ten months at the outside (some say after only two or three), their vitality is completely lost. By contact with putrescent fluids the bacilli are killed much more rapidly, even while their form remains unchanged, and they are still capable of being stained. Only in a very extreme case was putrefying tubercular sputum found to be capable of conveying disease after forty-three days. On the other hand, very low temperatures do not destroy, but only check, the vitality of the bacilli which remain capable of revival. I do not here speak of artificially high temperatures, or of antiseptics, since I am considering only conditions which may occur in nature.

The influence of light has been held to be important. Koch stated at the Berlin Medical Congress of 1890 that exposure of the bacilli to direct sunlight for a few days

* Baumgarten, *Lehrbuch der pathologischen Mykologie*, ii, 553. This work contains numerous references on the subject of the vitality of the tubercle bacillus.

destroys their vitality, but the precise experiments on which this statement was founded have not, I believe, been published.*

There can be no doubt that the conditions necessary for the preservation of the bacillus in a condition of quiescent vitality are present in climates such as ours. The question may arise, however, whether they are more likely to occur in the soil or in inhabited dwellings.

With regard to the open soil, whatever may be experimental possibilities, there is little concrete evidence for believing that it can be the nidus of the tubercle bacillus; that is that the tubercular virus is ever a soil-poison. For tuberculosis has never been known to be acquired by passing through a particular country, or sleeping in the open air, as in the case of ague; there is no evidence of its being communicated by accidental or intentional inoculation with earth, like tetanus; or by contaminated drinking-water like typhoid or cholera. Broadly speaking, its prevalence rises or falls with human, not with miasmatic conditions.

Dampness of Soil in Relation to Phthisis.

There is, however, one important condition of the soil, the connection of which with pulmonary consumption has been worked out by the classical researches of Sir George Buchanan, one of our former Presidents. He showed, by the law of concomitant variations (to use Mill's formula), that in certain portions of England the mortality from phthisis stood in a direct relation to the moisture of the subsoil; this being determined by the perviousness of the soil and the facilities for natural drainage. Further, he proved that a remarkable improvement in the death-rate from phthisis followed, in many English towns, the carrying out of extensive drainage-works, which had for their primary object the carrying off of sewage, but also led to drying of the subsoil. This result might be partly attributed to general sanitary improvements, especially as the lowering of the death-rate from typhoid fever was still

* These statements as to the injurious action of sunlight on the growth of the bacillus have not been confirmed by other investigators. Dr. Ransome (*Proceedings Royal Society*, xlix) found that exposure of tubercular sputum to light, *in conditions otherwise insanitary*, did not destroy its virulence, as tested by inoculation, but exposure to fresh air and light on a dry soil had that effect.

Sawizky found that dried tubercular sputum lost its virulence in two months and a half, but the change took place in the same time in darkness as when exposed to direct sunlight.

more striking; but it is extremely significant that *the death-rate from other pulmonary diseases did not diminish in the same ratio*, in most cases did not diminish at all, and in some instances was even increased, during the period to which these observations refer. The independent researches of Dr. Bowditch in America strikingly confirm these results.

A remarkable parallel to Sir G. Buchanan's results is presented by those recorded in a certain district of Germany by Dr. Finkelnburg, as presented to the *Congress für innere Medizin* at Wiesbaden, 1889 (*Berliner klinische Wochenschrift*, 1889, p. 434). The district of Meppen, in North Germany is a purely agricultural one, and among the most scantily populated in Germany. It is a moorland country, abounding in bogs, where the water collects. In this district the mortality from phthisis *in the female sex* is higher than in any other district. The same high rate of female phthisical mortality is, according to Dr. Finkelnburg, found in the adjacent parts of Holland and of Oldenburg; though in these parts the social conditions are different, and the only factor in common is the character of the soil. This excess of mortality from phthisis in the female sex has other bearings, which I shall refer to again.

On the other hand, it must be said there are several observations showing that in certain towns drainage has not diminished the death-rate from phthisis; and in some instances even an increased rate has followed such operations. And in certain districts of Sussex the diminution in mortality from phthisis, which was traced during the time of Sir G. Buchanan's observations, has been found by Dr. Kelly to be altered, or even inverted, in subsequent periods.

The laws of malaria, too, seem in some degree to contradict Sir G. Buchanan's conclusions. It has often been stated that malaria, or ague, which in our climate is so closely related to dampness of the soil, stands in an inverse ratio to phthisis as regards its prevalence in particular districts. This is a controverted point, on which I cannot enter; but one broad fact must not be forgotten, that malarious districts are, as a rule, thinly populated, while consumption is directly related to density of population; and hence, when certain districts are cleared of malaria, and become more thickly inhabited, phthisis is likely to assume a larger place in the statistics of mortality. Notwithstanding these objections, we cannot doubt that damp-

ness of soil is, on the whole, a favouring condition for the occurrence of phthisis. Whether it is so for other tubercular diseases, I am unable to say.

However, I wish to point out, as showing that tuberculosis cannot be strictly a soil-disease, that this influence is by no means a preponderating one, at least to the extent that it is in ague, in cholera, in typhoid, and some other maladies.

Ague has been notoriously almost exterminated in our own country during the last century, or, at the outside, two centuries; and there is nothing which can account for so universal a disappearance of the disease but the thorough drainage of the soil, which is regarded as an essential in modern agriculture.

But, with regard to phthisis, this is by no means the case. Nothing approaching to extinction of tubercular disease has been seen in any part of the country. The subsoil of London, for instance, is now remarkably dry, and must be getting drier every year, owing to the covering so large a proportion of the area with houses, and the remainder with pavements, almost or quite as impervious, so that only a small portion of the rainfall penetrates the soil at all. Except in our parks, gardens, unpaved yards, and the like, it is immediately carried off into the drains: a state of things which, over so large an area, can, I suppose, hardly be paralleled in the world, and which, even in our rainy climate, must inevitably tend, in the long run, to drying up of the subsoil, even to a considerable depth. Notwithstanding this, tubercular diseases, though they are decidedly diminishing, still flourish among us. On the whole, we cannot conclude that the condition of the soil is the main factor influencing the prevalence of tuberculosis, as would be the case were the virus of this disease a soil-poison.

Connection of Tubercular Disease with Dwellings.

It might be suggested that the influence of damp soil in favouring consumption is exerted by making the *houses* damp, and therefore unhealthy. I do not know any observations bearing on this point, beyond the general impression that "insanitary" dwellings foster tubercular disease. Of late years this question has assumed a somewhat different shape. It has been suggested, and in many instances proved, that a special prevalence of phthisis attaches to particular dwellings, so that special localities

in a town, special streets, special houses in a street, even special rooms in a house, have appeared to be nurseries of tubercular disease. This fact, I need hardly say, has been often observed in the case of other specific diseases. It was noticed in London, in Vienna, and other cities during successive invasions of the plague, in the seventeenth century, that the disease broke out in the same houses where it had prevailed in previous epidemics. With regard to typhus, diphtheria, and other infectious diseases, the fact is too well known to need dwelling upon. The question is, whether the same law holds with regard to tubercular diseases; that is, whether the infection, if it be called so, clings to particular houses, and not merely to houses having the same sanitary defects. That certain sanitary defects favour the occurrence of tuberculosis has, of course, been often pointed out. It has been shown unmistakably that imperfect ventilation and overcrowding of dwelling-houses or workshops greatly favour the prevalence of consumption. The often-told story of the high mortality from consumption in the English army, irrespective of climate, and the immense improvement which has resulted from improvements in barracks, is familiar to all. The excessive prevalence of the disease in prisons and asylums in former times, and the comparative exemption of such institutions at the present day, tell the same tale. Many histories of convents tell it still more clearly. From these facts was drawn a conclusion which has great influence on medical opinion as to the causation of phthisis; viz., that the breathing of air deteriorated by organic impurity, or, as some put it, of rebreathed air (to use the words of Sir James Clarke in 1835), is one of the most powerful favouring causes of the disease. The researches of Farr, McCormac, Parkes, Welch, and, more recently, of Dr. Arthur Ransome, Dr. Barry, and Mr. Gordon Smith, and others, have fully confirmed the earlier conclusions.

Before, however, committing ourselves to an unqualified faith in this theory, let us listen for a minute to a voice from the Antipodes. Mr. T. N. Fitzgerald, President of the Intercolonial Medical Congress, held at Melbourne, 1889, stated the results of his large practical experience as follows:—

"We have been long taught, rightly or wrongly, that scrofula and tubercle are affected by squalor and dirt; that phthisis is favoured by close vitiated atmosphere and cold night air. These causes are present but to a slight extent with us, yet occasionally we find scrofulous impregna-

tions excessively virulent; while phthisis is as common with us as it is in England; and decidedly more so than in Canada and Scotland."

* * * * *

"In my early days, it was impressed upon us that consumption chiefly arose from defective ventilation, and the inhalation of irritant particles. Then came the catarrhal or pneumonic origins, neglected colds, or so forth; and now we find that neither nor all of these reasons will suffice to account for the large bills of mortality from phthisis in this land.

"In my opinion, next to its hereditary inception, the greater part of phthisis will be found to be associated with defective drainage; and this, I believe, will be proved by bacteriology."*

There can be no doubt that the social status of the labouring class in the colonies is superior to that of the same class in this country; and that most of the conditions so often referred to are not widely prevalent there. Comfort is far more generally diffused, and the supply of food is generally abundant; while the milder climate does not encourage overcrowding in the same way as our humid skies and treacherous weather. Nevertheless, the death-rate from phthisis in Melbourne in 1885 was 2391.6 per 1,000,000 living; while in London, in 1887, it was only 1858 per million. The only circumstance in which Melbourne is comparable to the English cities half a century ago is the extremely defective state of the drainage.

It is possible that we exaggerate the force of these insanitary conditions; and it must not be forgotten that while the term "overcrowding" is modern, the fact which it denotes is ancient, not to say prehistoric. In cold countries it has always been the custom for men, as well as social animals, to huddle together at night for the sake of warmth. It is only latter-day ideas which make this a sanitary crime; while ventilation is distinctly a modern virtue. It seems to me difficult to regard these influences as more than favouring circumstances, aiding the operation of a cause more potent and more subtle. Admitting, however, the operation of such influences in this limited sense, their significance may be interpreted in two different ways.

Either these influences may act by deterioration of the general health, or by facilitating the conveyance of infec-

* Presidential Address to Intercolon. Med. Congress. Report, 1889, p. 13.

tion. The first mode of action is clearly seen in the influence which the same conditions have, for instance, in producing anæmia, which, apart from certain cases of developmental change, I believe to be produced in the labouring population of London far more directly by working in crowded, ill-ventilated rooms than by any other cause.

On the other hand, it may be a question of direct infection. No proof is needed that contagion increases in an intensified ratio with crowding in a limited space; it seems to be governed by a law like that of the inverse squares in the case of gravitation; and might probably receive a similar mathematical expression. Inductively, also, experience supplies abundant proof of the intensification of any contagion when confined within narrow limits.

This will be the case whether the infection is derived from an infected individual, or from any source of external infection.

It may be a question which of these explanations best accounts for the connection of tubercular disease with insanitary conditions of houses.

For my own part, I decidedly incline to the latter explanation: that the insanitary conditions of dwelling-houses, so far as they favour the spread and malignancy of tubercular disease, do so by fostering the growth of a specific contagion already present there; and the mere production of a cachectic state in the inhabitants, though it may be a contributory cause, is not sufficient to explain the facts.

In support of this conclusion I will review the evidence as to the existence of a specific infective agency in dwellings which have been observed to foster tubercular disease.

From my own experience I can say little about these relations. But some years ago I observed one case which impressed the possibility of such a connection very strongly upon my mind. A tradesman from a country town came to consult me, who had well-marked signs of phthisis. He was a well-built, robust man, in good circumstances, and was himself puzzled to understand why he should have become consumptive, considering his generally good constitution, and an entire absence of any family predisposition. He said he had been ill after moving from another town to that in which he then lived; and he was much impressed by the fact that two previous occupants of the house, quite unconnected with him by family, had died of consumption. There was one suspicious circumstance connected with the house, namely, that a well was sunk in the basement. This, of course, was a factor of dampness. Whether, therefore,

the determining cause of the phthisis was dampness, or whether it was an infection left by the previous occupants, I leave undetermined. There is no doubt as to the occurrence of sporadic instances like the solitary one which I have been able to contribute from my own experience. Such instances may easily be multiplied; and are only liable to the objection that in each case there may be mere coincidence—an objection which disappears when the numbers are considerable. Another group of facts is derived from the valuable researches of Dr. Arthur Ransome, detailed in a paper on "Some Evidences respecting Tubercular Infected Areas", contributed to the *Transactions of the Epidemiological Society* (vol. vi, N. S., p. 124).

Dr. Ransome says that his attention was first called to the subject by some striking instances of whole families *living in the same house* being carried off in succession by the disease; in one family of six members, the mother, an old woman, was the only survivor. In another, the only one, out of four or five, to escape was a daughter, who was in service elsewhere. He also quotes cases from the *Collective Investigation Record* to the same effect.

Three of these I will briefly refer to (Nos. 188, 194, 196). In each case a member of a previously healthy family came home ill of consumption, and several—*i.e.*, the majority—of the members of each family, though previously healthy, became affected with the disease and died of it within from two to six years.

Such cases, though many more might be quoted, are liable to the objection that family predisposition was the cause of the complaint. Greater weight, therefore, attaches to another case quoted in the *London Medical Record*, July 1884, on the authority of Dr. Kempf, of Louisville, U.S., in which phthisis appeared to be introduced into a convent, said to be well situated and ventilated, with the result that, within four months, nine sisters, regarded as exceptionally healthy, became consumptive, and four died in the course of the year. After complete isolation of the sick the epidemic was stopped. Dr. Ransome justly expresses some doubt as to the sanitary condition of the convent; but still, the fact of the introduction of the disease into a building, and its eradication (by preventive measures), is not weakened thereby. Dr. Ransome's account of the prevalence of phthisis in certain streets of badly-built houses, deficient in supply of fresh air, is most striking. But what I particularly select from his statistics is the number of instances in which two or more deaths from

phthisis occurred in the same house. "Altogether", he says, "there were twenty-one such coincidences", and fifteen of them (thirty deaths in all) occurred in narrow streets, culs-de-sac, or small courts. This was in a district in Ancoats, Manchester, in a period of five years.

In a district in Greengate (Salford) eight deaths were in four houses, or four coincidences. In another district, out of forty cases in six years, ten were in five houses. The distribution of these deaths as to families is not given.

In his Milroy Lectures "On the Causes and Prevention of Phthisis" (p. 65), Dr. Ransome quotes also a personal communication from Dr. Niven of Oldham, showing that out of 3,001 deaths from tuberculosis during eleven years, in 302 instances there were two or more in a house. Dr. Niven calculates mathematically that the chance of any house being twice affected (independent of infection), only 68 houses would have suffered, whereas 274 were thus attacked, and that whilst not more than 7.6 houses should have suffered thrice, the actual number so attacked was 24.

Dr. Ransome also gives the following results arrived at by Dr. Flick of Philadelphia (whose original memoir I have not been able to meet with), from a minute topographical study of phthisis in that city during 25 years:—

(1) A house which has had one case of consumption will probably have another within five years, and may have a large number of cases in close succession.

(2) When a case of consumption occurs in a house, approximate houses are considerably exposed to contagion.

(3) Houses in *localities* where endemic after endemic has existed, have nevertheless escaped the disease.

(4) Tuberculosis of different kinds occurs in the same localities, and often on the same lots as consumption.

(5) During the twenty-five years, scarcely 20 per cent. of the houses of the ward were so affected.

He ascribes these results to contagion in the houses themselves.

Another still more important class of cases is that in which a house or room which has been occupied by a patient with phthisis gives rise to tubercular disease in subsequent occupants.

Dr. Janeway of New York (*Archives of Medicine*, quoted in *Brit. Med. Journal*, 1883, i, 377) gives the following case:—

"A gentleman died of phthisis after two years' illness, in February 1882. His sister and her husband occupied his room after his death. The brother-in-law began to fail

five weeks afterwards, and in May was the subject of acute phthisis."

Dr. Burney Yeo mentions, among others, the following (*Brit. Med. Journal*, 1885, i, 774):—

"A fine young Scotch girl, of a healthy, long-lived family, was afflicted with phthisis. On enquiry it was found that some few months before she had been given a bedroom which had just been quitted by a maidservant with phthisis."

Dr. Niven (*Public Health*, ii, 206) gives a very similar case:—

"A married woman from Oldham went with two children (one a lad ten years old) to Southport, to join her husband, in September 1887. The husband, wife, and the two children all slept in one front room. In the same house was a woman suffering from consumption, said to have been contracted from her husband, who had previously died of the same disease. As the weather got colder, this consumptive woman asked them to change rooms with her, as her bedroom was colder than theirs. This was done. The Oldham woman used to complain of a peculiar odour in the room, which does not seem to have had any special cleansing or disinfection. In January 1888, the boy, ten years old, died of 'inflammation of the brain'; he had been ill a month, and from the history, his fatal malady was almost certainly tubercular meningitis. The Oldham woman became pregnant in Southport, but removed shortly afterwards to Oldham, and was there confined in June 1888; but before the birth of the baby she lost flesh, and showed the first symptoms of phthisis. The baby died in June 1889, of tabes mesenterica, and she died in October, of phthisis."

Another illustration is quoted by Dr. Heron (*Evidences of the Communicability of Consumption*, 1890, Appendix, p. 153) from Kruche (*Deutsche Med. Zeitung*, 1882, p. 445):—

"A young robust lawyer spent some time at a health-resort; and some weeks after his return home showed symptoms of a rapidly fatal attack of consumption. It was found on inquiry that in the place referred to he had occupied a room and bed just vacated by a consumptive, who had suffered from suppurating sores."

The most striking example of this mode of communication which I have met with is related by F. Engelmann (*Berlin. klin. Wochenschrift*, 1889, Jan. 7, p. 6), and relates to a particular dwelling (or "flat") in a large house occupied

by the families of several glass-blowers employed in a certain factory. This occupation is one known to produce remarkable liability to phthisis; and Engelmann believes that 75 to 80 per cent. of the workmen in this particular place die of it. It is well known that this frequently has been ascribed, among other causes, to direct infection from mouth to mouth by the blow-pipe. However, that would not explain the special incidences here described. The house was built about 1865, and was generally in tolerable sanitary condition. The particular dwelling in question was badly ventilated and lighted. It was occupied from 1865 to 1873 by three families in succession who were all healthy. In 1874 a family named Nestle entered, in which the mother was already consumptive, and had lost a son from the same disease. She died there from hæmoptysis, and shortly afterwards the family left, having lived there for one year only. The next occupants were a family (Gotz) of seven persons, all in good health, though there was a history of chest disease in the mother's family. After one year's residence in this dwelling they left, and at a later time it was found that the father, mother, and one son had died of phthisis, and a fine boy of chronic peritonitis. The third family (Gunnel) occupying the dwelling were healthy on arrival, and had no hereditary taint. A child born in the house died of meningitis; another child died of "marasmus"; another boy acquired hip-joint disease. Later on, the father died of phthisis, and another child of meningitis; the mother became phthisical; and a surviving girl is extremely scrofulous.

A fourth family (Hübchen) came in after the last mentioned, all healthy. The mother became phthisical, and bacilli were detected in the sputum. Two children died of meningitis under one year old.

Summing up the history, it appears that for eight years, 1865-73, the dwelling was free from tubercular disease. Then came one year's tenancy by a person already tuberculous. After this, in a period of twelve years, at least twelve cases of tubercular disease were traced to this source.

It is noted that the dwelling was never vacant, the new tenants entering while it was, so to speak, still warm from the last; and during the whole period it was never painted or cleaned.

Engelmann asserts that this neglect did not occur in other parts of the same large house; and that no similar

instance of tubercular disease clinging to a dwelling was observed in them.*

The gigantic literature of tuberculosis, if sifted, would, no doubt, supply other similar instances; but as it is on an occasion like this impossible to be exhaustive, I will only assume that the evidence adduced proves that the tubercular infection is sometimes found to attach itself to houses; and that in some cases this infection is clearly traceable, as in acute contagious diseases, to contamination by a previous occupant. Even in cases where this cannot be proved, there is nothing to contradict the hypothesis that the infection may have been originally introduced by a tubercular individual. If, on the other hand, we should have instances of what is presumably tubercular house-infection, occurring in *new houses*, then, however unhealthy the situation, it would tell against this hypothesis, and would rather point to a miasmatic or ectogenic habitat of the bacillus.

It is clear that the hypothesis of house-infection is quite adequate also to explain cases attributed to direct personal contagion; since a present and living tubercular patient must contaminate a house or room even more certainly that one dead or departed.

As an instance of such cases I quote the following (*Collective Investigation Record*, 1883):—

"Miss R., aged 48, a dressmaker, living in a rather lonely cottage in Bedfordshire, had three apprentices, young girls of from 17 to 19 years of age, not related, from three adjacent villages, who took it in turn to remain in the

* Since writing the above, I have come across another paper by Dr. Niven of Oldham (*Public Health*, vol iii, p. 463), containing notes of cases in which exposure to infection of tubercular disease was ascertained. From these I extract the following as bearing on house-infection, carefully omitting all cases of relationship:—

No. 17, man of 22. Previous tenant in the house where he contracted the disease died of consumption in 1886. House damp, unhealthy.

No. 34, child of 4 months, died in a house where previous occupants died of consumption, but child only lived five weeks in this house.

No. 57, man aged 24. After five years' illness, previous to which time he had lodged with a consumptive young man.

No. 95. Lodged with a person who since became consumptive six years before. This period seems too long to account for the infection of either.

Dr. Niven states that his further researches into the occurrence of second deaths from tuberculosis in the same house do not yield so much information as might be expected. He thinks the facts suggest that the infection does not, as a rule, remain in a house sufficiently long to be dangerous to new occupants.

Dr. Niven, in an address reported in *Practitioner*, 1889, ii, 223, gives other cases where there was a probability of infection having been acquired in a particular house. The numbers were six out of forty-one houses, or about one-seventh. Still, in all these cases, as I understand, the element of family relationship also came into play.

house, and slept with her, each one for a week at a time. During their apprenticeship Miss R. was taken with phthisis, of which she died. In less than two years afterwards, all three apprentices died of phthisis, though no trace of this disease appeared in the family history of any of them; and the parents, brothers, and sisters of two of them are alive and well at the present day."

I quote this case particularly since it has been criticised by Dr. Andrew, in his able Lumleian Lectures on the Causation of Phthisis (*Brit. Med. Journal*, 1884, i, p. 754), as inconclusive, because the three apprentices did not communicate the disease to their own families; and he regards it is unlikely that there should have been a special virulence in the first case which was wanting in the other three. The answer is, I think, that the house inhabited by Miss R. had become converted into a focus of contagion. The circumstances in the three families to which the apprentices belonged, we do not know; nor even whether they died of phthisis in their own families; but very probably the conditions necessary to make their houses foci of contagion were wanting.

Although I have purposely avoided quoting cases of multiple occurrence of phthisis in families, and especially the numerous instances of coincidences of the disease in husbands and wives, as instances of the effect of house-infection, it is clear that they can be accounted for on this theory with great facility; since, as a rule, the inhabitants of one house belong to one family. And even the supposition of a family predisposition to infection does not enfeeble the argument; since no infection spreads inevitably, and there must be some reason why one person is infected rather than another; while in contagious diseases like diphtheria and typhoid a family predisposition, irrespective of contagion, is often displayed. The hypothesis of direct inheritance, if clearly established, is the only one which makes all others unnecessary.

Another remarkable law which, on the principle of concomitant variations, tells in favour of house-infection, is the preponderance of phthisis in the female sex *among agricultural populations*, while the inverse proportion obtains in town. This fact is so well ascertained in our own country as to be beyond dispute. An excellent table is given in Dr. Ransome's Milroy Lectures (p. 39), showing twelve country districts with an excess of female phthisis, and nine town districts with an excess on the male side. The statistics of Meppen, formerly referred to, exhibit the

same law. It is stated in Dr. Wilson Fox's work on *Diseases of the Lungs*, on the authority of Walshe, that, in certain malarious districts, the women who do not work in the fields are the only sufferers from phthisis.

The explanation generally given of this difference is that the outdoor life of men is healthier, and therefore antagonistic to phthisis. But it is as logical to say that the indoor life of women exposes them to some injurious influence derived from the house itself.*

Further, it may be observed that in the case of cattle the connection of tubercular disease with particular buildings, or even with particular stalls in a building, has often been observed, and is regarded as an established fact. Moreover, in the case of rabbits, or other rodents kept for experimental purposes, the production of tuberculosis in them by infection of the places in which they are kept is a well-recognised occurrence. This was the cause of the experimental fallacies which led to the belief that tubercle could be produced in animals by the inoculation of inflammatory non-specific material. Cohnheim found that he could produce tubercle by this kind of inoculation in rabbits in the Pathological Institute at Berlin, but when he removed to Würzburg these experiments no longer succeeded. The explanation was that the cages for rabbits, etc. in Berlin had become permanently infected with tubercle, and it has been recognised by Dr. Burdon Sanderson and the late Dr. Wilson Fox that the same explanation applied to their results.

* The significance of this difference is not diminished, but enhanced, by the results of a valuable table on the relative liability of the two sexes to pulmonary phthisis, contributed to the same work (p. 519) by Dr. William Ogle. Dr. Ogle shows that, taking the country as a whole, this liability is the same for the two sexes when all question of age is put aside; but this equality does not extend to other tubercular diseases, under which headings the male death-rate is at all periods of life in excess of the female. This excess, too, is especially marked in the early years of life (when children of both sexes live equally in the house), the death-rate of male children from these diseases being for the first five years decidedly higher than that of females; the mean annual mortality from all tubercular diseases of one million children under five being, for males, 5,385, for females, 4,264, or an excess on the male side of more than 25 per cent. As regards phthisis alone, he finds that the male death-rate in the first year of life is more than twice as high as the female rate. In the second year it is still slightly higher, but in the third year the female death-rate begins to exceed the male, and continues to be in excess up to about 35 years of age, after which the male rate preponderates. This excess on the female side is especially marked in the period from ten to twenty years, when it amounts to 50 per cent. Now it is at this period of life that the difference between the outdoor life of boys and the indoor life of girls begins. The greater liability of the male sex to phthisis after 35 years of age seems, however, to be quite unexplained by such considerations.

Numerous direct observations have been made to the same effect; so that this is a danger well recognised in all such experimental researches, and guarded against with corresponding care. From the above evidence I think we may conclude that the tubercular infection is frequently found in houses, and that by residence in such houses human beings may become infected. Further, there is no reason to suppose that the bacilli, by which they become so, have had any other origin than from men, or possibly domestic animals, affected with the tubercular disease. How long such infection may persist we do not know.

Mode of Tubercular Infection from Houses.

The precise manner in which infection is acquired from dwellings has been much discussed, but the most definite results have been obtained by the researches of Dr. Cornet* and others who have followed his methods. To give a full account of his results would occupy too long. I can only glance at a few of the facts which he has collected.

His method consisted in removing small quantities of dust from the floor and walls of hospital wards, the private houses of phthisical patients, and other buildings; either with a platinum spatula, or by rubbing the wall with a sterilised sponge. The materials thus obtained were mixed with a small quantity of sterilized bouillon or distilled water, and injected into the peritoneal cavity of guinea-pigs, the utmost care being taken to avoid accidental infection, and to take animals which were free from disease; although a previously acquired tuberculosis is easily distinguished in these animals from an inoculated one. The method of inoculation is, I need hardly say, now recognised as a much more delicate test for the presence of tubercular infective material than microscopical examination for bacilli. In fact, in specimens of dust thus proved to be capable of transmitting tubercle, no bacilli could be detected, which, of course, does not by any means show that none were present, but that they were few in number, or else in the state of spores.

The part of the room chosen for investigation was one near the phthisical patient, but not one where sputum could have been directly deposited; and sometimes parts of the bedstead were also examined.

* *Ueber Tuberkulose*, von Dr. Georg Cornet. Leipzig, 1890.

Some of Cornet's results are very instructive. First, as a negative conclusion, Cornet's researches give no support to the prevalent impression which we often hear expressed in an exaggerated form, that the tubercular virus is universally distributed in cities, in houses, or even in hospital wards. Out of seven hospitals investigated, five gave positive results, that is, a certain proportion of the animals inoculated with dust or other products became tuberculous. In some cases the animals died of some intercurrent disease, such as peritonitis or malignant œdema, showing that the dust contained infective material.

Specimens from three lunatic asylums, and from rooms where phthisical patients lived or had lately lived, gave positive results in a smaller proportion. Specimens from the dwellings of private consumptive patients gave positive results in nearly half the number of cases. What is very striking is that specimens from hospital out-patients' rooms, from a hospital for skin diseases where there were patients affected with lupus, from surgical wards, and from the Pathological Institute and an Orphan Asylum, all gave negative results as regards tubercular infection. As a further control experiment, specimens were taken from several public buildings, from the outer walls of houses in frequented streets, and from street dust, all of which gave no tubercular infection, though in many cases other diseases were produced.

The general result was to show that in many cases the places where phthisical patients contain dust which is capable of communicating tubercle by inoculation.

The negative results from other buildings and places could not, of course, prove that no tubercular material was there, but only that it was not universally distributed.

To a certain extent these results appear consoling, since it has been of late years so much the custom to assume that in cities, at all events, one is in continual danger of breathing in tubercle bacilli, and that we must all of us have many times had tubercle bacilli in our mouths or air-passages. Not, of course, that they exclude the possibility of infection by the most remote channels, but they indicate from what quarter infection is likely to come, if it does come.

Krüger has confirmed Cornet's results by investigations carried out at Bonn.

The chief objections to his views are drawn from the theoretical considerations that other modes of acquiring tubercular disease must exist, and are more important;

some authorities, as Baumgarten, trying to prove that tubercle is mainly inherited, and others that food in some form is the chief means of communicating the disease.

Is tubercular disease acquired by inhalation of bacilli?—Cornet's views on the spread of tuberculosis, as deduced from his experiments, lay an almost exclusive weight on infection of the lungs by inhalation of tubercle bacilli, which must be so dry as to be carried about with dust, and hence he regards moisture of walls and floors as a condition hindering, not favouring, the spread of infection. That tubercular sputum does contain the virus of tubercle in a very potent form is proved "up to the hilt" by countless inoculation experiments. It is not too much to say that the production of tuberculosis by this means in rodents is as certain as the communication of cow-pox by vaccine lymph.

Still the question is whether this is the chief means of spreading tubercular disease among mankind; and this resolves itself into two questions: first, whether the sputum is the chief means by which tubercle-infection leaves the body; and secondly, whether inhalation is the chief means by which it is received. The one does not quite necessarily follow from the other.

(1) As to the first question, it would seem that if the tubercle bacillus be regarded as a parasite, such a means of continuing its species is in accordance with the general laws of parasitism, and similar to those methods which animal parasites unconsciously adopt for the continuance of their species. Consider the case of a tapeworm continually expelling its eggs, amounting to many thousands in a year, from the intestines of its host; though only one here and there arrives at a destination where it is able to develop into a cysticercus; and even out of this number very few again are likely to undergo further development into a tapeworm.

Consider, then, the expulsion of tubercle bacilli from the lungs in numbers counted by millions (twenty millions in twenty-four hours, according to Bollinger), as compared to thousands in the other case; and suppose that only one here and there arrives in another body where it can develop: is not this *comparatis comparandis* a very similar case? Why, we may ask, should the tubercular parasite plant itself in this particular part of the body, and set up a chain of processes which, if regarded as intentional, would be a mechanism admirably constructed to facilitate the passage of the species from one host to another? It is self-evident that these

processes are not intentional, in any sense in which that word can be used; but still, they may be the result of an inherited habit, impressed upon the bacillus in the course of its evolution through countless generations by which its existence as a parasitic species has become established. I have elsewhere* drawn attention to the fact that all the habits of animal parasites, the way in which they enter the body of their hosts, the part of the body to which they direct themselves, and the channel by which they leave it, all tend to the preservation of the race as a parasitic species, and, if contrived deliberately for that end, would be regarded as admirably adapted for the purpose. Thus the hydatid cyst is developed in the liver, the trichina spiralis passes into muscle; and thus both find their way, with food, into the bowels of their carnivorous host, where they undergo their next development.

Thus, too, the egg of the tapeworm finds its way into the water, with which it enters the body of that host in which it has to pass through its next stage of existence.

The law is, I believe, the same for vegetable parasites, such as the bacteria which constitute the contagia of specific diseases. They must enter the body by a suitable channel, and pass to a part from which they can again leave the body in such a way as to continue the race. Thus the air-borne contagia of scarlatina and small-pox are determined to the skin, from which they pass into the air again; the contagia of cholera and enteric fever pass out from the bowels into the soil and water; each passing into the medium best adapted to facilitate its passage into the next host, and thus secure the continuance of the race. In soil-diseases, such as ague, not communicable from man to man, we should not expect to find any elimination of the contagium or germ; and the *Plasmodium malariæ* of Laveran, which is not known to pass out of the body by any channel, certainly fulfils this negative condition.

The fact of the elimination of tubercular contagium on a large scale from diseased persons certainly, so far as it goes, points to the conclusion that tuberculosis is not a soil-disease (as suggested, for instance, by Dr. Andrew in his Lumleian Lectures), but belongs to the contagious family.

Another reason for thinking that the lung is the predominant, or one might say, figuratively, the appointed channel for the elimination of the tubercle bacillus, and consequent preservation of the parasitic race, is that by

* "Specific Diseases considered with reference to the Laws of Parasitism"; *St. Thomas's Hospital Reports*, vol. xx.

whatever means the bacillus enters the body, it ultimately, in a great majority of cases, affects the lungs. Louis's old law, that if tubercle is found anywhere in the body, it is found also in the lungs, still remains nearly true; the exceptions being chiefly in so-called scrofulous affections; though even these may produce general tuberculosis. Another still more cogent fact is that the experimental tuberculosis of animals, whether brought about by inoculation or by tubercular food, nearly always produces pulmonary tubercle as a secondary lesion; perhaps always, if the animals live long enough; and this even when the primary lesion is small or inconspicuous. This is attested by all experimenters, from Villemin onwards.

(2) But the question whether inhalation of dried sputum into the lungs is *the chief means* by which tubercular disease is acquired is a very different one.

Against the assumption there are many weighty arguments, which have been forcibly urged by Baumgarten and others.

First, the artificial production of tubercular disease in animals by inhalation, though it has been actually effected, is a very difficult process.

Many experiments in this direction have completely failed, though Tappeiner, Klein, and others have obtained positive results. Tappeiner's were obtained by a special and difficult method. He shut up the experimental animals in a box or chamber, into which large quantities of tubercular sputum were discharged in the form of spray by a special apparatus, and found that they all became tuberculous. It may be said that such a concentration of virus does not occur in nature. An unfortunate occurrence showed, however, that infection of the human subject by this means was possible. The servant who had charge of Tappeiner's apparatus, in spite of the most forcible and serious warnings, persisted, by way of bravado, in entering the inhalation chamber. He was a very robust man, in perfect health, and without the slightest hereditary tendency to consumption. Nevertheless, he paid the penalty of his rashness by acquiring an acute tuberculosis, which carried him off in fourteen weeks, producing typical morbid appearances in the body.*

One positive fact outweighs many negative, and this would be enough to show the possibility of infection by inhalation; though such conditions may be hardly likely to occur in ordinary life. The inhalation of tubercular material

* Cornet, *Tuberkulose*, p. 117; from *Schweninger gesammelte Arbeiten*, Berlin, 1886, Bd. i.

sufficient to produce disease must, it may be conceded, be somewhat occasional, and governed by circumstances which can only be called accidental. Nevertheless, accidents will happen. Some may think, with Cornet, that inhalation accounts for the greater part of tubercular diseases. Some may think, with Baumgarten, that it explains only a small part. It seems impossible to deny that it explains a certain part. Supposing, however, it be proved that the sputum of phthisical persons sets free a large quantity of virulent material, is there no other way than inhalation by which this material can enter the human body?

There is certainly one other, that is, with food into the digestive channels. This must be a possible means, as seen in the rare cases of infection with typhoid or cholera of those who attend in sick-rooms, and who cannot be supposed to inhale the organisms of these diseases. It must be a rare case with adults; but for children seems not so impossible. Considering the habits of children, one can see how they might, in the crowded dwellings of the poor, pollute their articles of food with tubercular material scattered about the room of a phthisical parent, or other inmate. Among the causes of intestinal tubercular disease, so frequent in children of phthisical families among the working classes, this possibility should not, it seems to me, be forgotten.

There is, again, the possibility of inoculation; a well-known, though rare, means of acquiring the disease from a previous case of tuberculosis. This undoubtedly happens sometimes, but can hardly be a main factor in the continued existence of the bacillus.

Putting all these possibilities together, it may still seem that the probability of contagion, direct or indirect, is small compared with the probability which there is in the case of the diseases commonly called contagious. Moreover, the very word contagious calls up a group of relations which we cannot trace in tubercular disease, and which prejudice us against the reception of the idea. We think at once of scarlatina, measles, small-pox, and so on, in which the contagion may be briefly characterised as direct, easily traceable, and momentary; while the communication of tubercle, if it occurs, will be indirect, untraceable, and possibly requiring time for its completion.

But there is one consideration lost sight of in contrasting the communicability of tubercle with that of the acute specific diseases, and that is the element of *time*.

The period of contagiosity in acute disease is measured

by days or weeks, that of tubercular disease by years. A patient with measles or small-pox emits an extremely virulent contagium during, say, three to six weeks, and the possibilities of transmitting the disease are in the main limited to that period of time.

On the other hand, a patient with phthisis goes on expectorating a much less virulent contagium, with fewer possibilities of transmission; but the process goes on for two or three years. Is it not possible that the longer duration of contagiosity may make up for its lower degree? The final result, as regards possibility of transmission, might be, if not equal, at all events sufficiently nearly so to be comparable. The total contagiosity, that is, the possibility of existence or *viability* of the specific micro-organism, is a function of two variables, duration and intensity; so that a high value for one of these variables may make up for a low value of the other. If the acute specific fevers had only a low degree of contagiosity they would probably cease to exist, so far as man is concerned, or, at least, cease to be transmitted (though their living causes might have another mode of existence).

But if tubercular disease had the degree of contagiosity seen in the acute specifics, the results, as regards its diffusion in the world, would be very different from what they are, and much more disastrous.

Hence a comparatively low degree of contagiosity for tubercle might still suffice to explain its continued existence, more especially if reinforced by other factors which I will now proceed to consider.

Hereditary Transmission of Tubercle.

There is another way, quite different from infection, in which a specific disease might be kept alive and remain endemic in any country or population: that is, by inheritance.

Let it once be granted that tubercular disease may be transmitted directly from parent to offspring, and a considerable proportion of the cases of disease might be explained.

The heredity of tubercular disease is a vast problem which can only be briefly touched upon here; but the broad fact that the children of tuberculous parents are, on the whole, more likely than others to become tuberculous, has never been doubted, at least in modern times. Two

explanations may, however, be given of this fact. The one, which has been till lately the only accepted theory, is that what is inherited is a particular predisposition or tendency, by which members of tubercular families are more likely than others to acquire tubercular disease when exposed to any of its causes.

But since the discovery of the specific nature of tubercle, another theory, that of *direct inheritance*, has been proposed, of which Cohnheim was, I believe, the originator; and Baumgarten is now the chief supporter. It supposes that the germ of disease (*i.e.*, the bacillus) is directly transmitted either from the male or female parent, just as we know the germ of syphilis is transmitted, even though the precise nature of the latter is unknown.

In the case of syphilis the proof of such transmission rests upon the occasional presence of signs of the disease in the newly-born child, or the immature fœtus; and also on the occurrence at later periods of manifestations of syphilis belonging to the secondary or tertiary stage, even when strictly congenital symptoms were not observed, or perhaps did not exist, and contagion was out of the question. If the case of tubercle were parallel, we ought to be able to find occasionally evidence of fœtal or strictly congenital tuberculosis, and more frequently evidence of the development of the disease in early or adult life in circumstances under which direct acquisition of the disease was, to say the least, improbable.

Congenital or Fœtal Tuberculosis.

A strong argument for the possibility of fœtal tuberculosis in man is derived from the fact that it undoubtedly occurs in cattle.

There are now a considerable number of well-established cases where fœtal or newly-born calves have been found presenting characteristic lesions of tubercle, and in some of them the occurrence of tubercle in the mother was well established. In a smaller number of instances, I think, on the whole, tubercular disease was found to be present in the sire.

This is the more remarkable, as tubercle is very rare in calves at the age at which they are generally killed for the market: the development of the disease not usually occurring in cattle till the second year, or later.

A very small number of similar instances have been observed in human infants.

A definite observation of tubercle in a newly-born child was reported by Hiller to the Medical Congress at Copenhagen in 1884. Demme found tubercle of the thymus in a child dying at six weeks old, which, from the inaccessibility of that organ, could hardly have been acquired.*

A well-marked case of tubercle in the tissues of a fœtus removed by Cæsarean section from the body of a mother who shortly afterwards died from acute tuberculosis is recorded by Birch-Hirschfeld. Tubercle bacilli were detected in the fœtal liver, and the presence of the virus was proved in other organs by inoculations into animals. The bacilli were also found in both the maternal and fœtal portions of the placenta, showing that they were capable of passing through that organ.†

In the discussion on Birch-Hirschfeld's case, Rindfleisch reported a quite similar one.‡

In the last two cases the method of transmission was apparently through the placenta, which is not the same thing as deposition of bacilli in the ovum.

It has also been shown that the infective virus of tubercle may be contained in the tissues of the newly-born infant of a phthisical mother, even when the infant shows no visible tubercle (Landouzy and Martin), though it must be admitted that many experiments in this direction have failed. Landouzy has reported another case of the same kind in the five-months-old (abortive) fœtus of a phthisical mother. Transmission of the disease from the male parent direct to the ovum is also probable, though, from the nature of the case, less easily demonstrated. Tubercle bacilli have been found in the testicles or seminal vesicles of men dying from phthisis, even when those organs were free from disease (Jani); and such facts may also explain the occasional transmission of tubercular disease from husband to wife. Experiments to test by inoculation the infective power of the semen in similar cases in the human subject have in several cases given only negative results: but the semen of tubercular guinea-pigs was found by Landouzy to be infective in six cases out of sixteen.

Another line of evidence is derived from the presence of tubercle in very young children, in whom infection from without was, at all events, very improbable, if not absolutely excluded. There is, or was till lately, an impression

* For reference to a few other cases of the kind, see Dr. J. E. Squire's elaborate paper in our *Transactions* for 1888-9 (vol. viii, p. 51).

† *Wiener Mediz. Blätter*, No. 17, 1891.

‡ Baumgarten's *Jahresbericht*, 1890, p. 299.

among pathologists that tubercular disease is very rare in infants during the first year of life. But this may depend partly on the fact that children's hospitals do not admit many children so young, and that, consequently, few *post-mortem* examinations are made of infants dying at this age. The earliest instance in my own experience was that of a child who suffered (as was alleged, from the time of birth) from a scrofulous abscess, which ended at the age of four months in general tuberculosis. But in my experience such cases are not common, and their rarity is borne out by the results of the *post-mortem* examination of a number of still-born children made by my friend Dr. Cory. In one hundred bodies thus examined he never found any visible tubercular disease, though signs of congenital syphilis were sometimes present.* Dr. Cory informs me that a second series of one hundred cases has given equally negative results as regards tubercular disease. Considering that these statistics were collected in the Maternity Department of St. Thomas's Hospital in the south of London, from a population among whom tubercular disease is certainly widely prevalent, they are undoubtedly of some weight as showing that strictly congenital tubercular disease is far from common, and can hardly be an important factor in keeping alive the disease as an endemic.

Moreover, it will appear on reflection that tubercle developing thus early in life will have a very small chance of being transmitted to the next generation. For the infants thus affected will mostly die long before the age of reproduction; or, if they survive, it can only be on condition of the disease being completely cured, so as to be, we may presume, incapable of transmission. Infantile tuberculosis, if fatal to the subjects, will also be fatal to the bacilli producing it. Also, the chance of spreading the disease by infection will be much less in the case of infants than in that of adults. Young children do not expectorate, and if they did eliminate the bacilli in any numbers, their relations to society are so much more limited than those of adults, that the probabilities of infection are fewer. On the whole, then, from the point of view of the tubercle bacillus, the production of infantile or congenital tuberculosis is not a hopeful direction in which to propagate its race. Bacilli which had this habit of early development would die out, and the continuance of the species bacillus

* Cory, *St. Thomas's Hospital Reports*, vol. viii, p. 61, and vol. x, p. 263.

would be arrested so far as that particular strain was concerned.

Latency of the Tubercle Bacillus.

Baumgarten's theory of hereditary transmission of the bacillus requires another condition in its natural history. It assumes that the bacillus may remain latent in the human body, in the form of spores or some inactive state, till the period of adolescence or early adult life. He supposes that the growing tissues may exert an inhibitory effect on the growth of the bacillus, which will therefore only begin to develop when the period of growth is past. If it become active at this period of human life, it will have a chance of being further transmitted by inheritance (since tubercular individuals are by no means deficient in fertility or averse to matrimony); and will also have many more chances of being transmitted by indirect contagion (by expectoration and otherwise) than in the case of an infantile disease.

It would certainly seem, *à priori*, that the best chances for inherited bacilli, of transmitting their race, would be given, if they remained latent in the human body till adult life. The question is, whether we have any reason to believe that the bacilli may have this property or habit of latency.

It may seem at first sight very improbable that this should be the case. Nevertheless, such a fact would not be without analogy. The disease of silkworms called *pébrine*, has been shown to be caused by a micro-organism, which may be transmitted by contagion, and also by inheritance, to the eggs. In the latter case the eggs may be hatched, and the worm go through several changes, but its development is gradually arrested, and it dies, when its body is found to be filled with the microbes. On Baumgarten's theory, tubercle is a sort of *pébrine* of the human race; the inherited germ becoming incorporated with the ovum, but not destroying it, and not producing obvious disease till a more or less advanced stage of development is reached; while, like the silkworm disease, it has also another mode of transmission by external contagion.

In either disease, if the parasitic organism were fatal to its host at too early a period of development, hereditary transmission through more than one generation could not occur.

Furthermore, if we suppose that this late development

or prolonged latency were a sort of *habit* of the parasitic micro-organism, we may see, on the principle of natural selection, that the habit might become permanently fixed in the bacillus. For those which developed late would have a much better chance of perpetuating their race than those which developed early; the latter, indeed, soon dying out. Thus the property of prolonged latency might become a permanent feature in the biology of the bacillus.*

In cattle, among which the continuance of tuberculosis, especially as regards inheritance, seems to be more certain and uniform than in the human race, the tendency to late development of this disease is most marked. This is shown in the first place by the great rarity of tubercle in calves slaughtered for food, as compared with its frequency in adult cattle; and is supported also, though less conclusively, by its greater frequency in cows than in bullocks, as observed in slaughter-houses. Bullocks being bred for the purposes of food are seldom allowed to live beyond the third year; while cows are generally killed for food after they have served for reproduction, and for giving milk: consequently their average age at death is much higher. The circumstance which weakens the force of this argument is that cows, being kept in stalls, live in less healthy conditions than young bullocks, which spend a great part of their life in open pastures. On the other hand, a good many bullocks are fed for the market in stalls, in conditions favourable to the development of tubercle. But to what proportion of beasts this applies, or how much of their life is spent in these conditions, I am quite unable to say. Bulls kept for breeding, also, of course, live longer than oxen killed for the market; and it is asserted that tuberculosis is very common among the former class of animals; but I am not acquainted with any statistics showing its relative or absolute frequency.

* The effect of heredity, combined with late development, in causing the spread of a disease, is indeed, as it seems, actually traceable in the case of cancer. In the *Report of the Registrar-General for* 1889, Dr. Ogle points out that the mortality attributed to cancer is constantly increasing, and that, assuming the disease to be hereditary, as is generally, though not universally, accepted; and if, as undoubtedly is the case, "its development does not, as a rule, manifest itself till after the usual age of marriage and reproduction, it must follow, as a necessary arithmetical consequence, that the tendency shall spread wider and wider among the population." By arguments similar to those here used, it is shown that this will not apply to tubercular phthisis. (*Report*, p. xiii.)

If, however, the laws of inherited tubercle are such as have been here suggested, tuberculosis would be analogous to cancer in this respect.

Objections to the Theory of Latency.

Many objections have been made to Baumgarten's theory of the latency of inherited tuberculosis. For one thing, it may be said that the presence of tubercle bacilli, or their spores, in the ovum, must inevitably check its development and prevent it from arriving at maturity, if impregnated. Whether this would or would not be the case, is difficult to say, on *à priori* grounds.

As an analogy, we may recall the facts of inherited syphilis. When the syphilitic virus derived from either parent affects the impregnated ovum, it does not necessarily destroy its vitality. Abortion may occur, but in most cases the fœtus is completely formed, and, when born, generally shows at first no sign of the disease. But after birth the virus begins to develop, so that at a period after birth corresponding to the known incubation of the disease when acquired, the first signs of the disease, such as eruptions on the skin, etc., appear. It would seem as if the fœtal tissues exercised an inhibitory effect on the development of the syphilitic virus.

There are also some remarkable experiments bearing upon the effects of bacillary infection of an ovum, namely, those of Maffucci on hens' eggs. He introduced into impregnated eggs certain species of bacteria, choosing those which were known to affect the adult fowl. He found that these, especially pathogenic forms, were unable to grow in the tissues of the embryo, though they did not interfere with its development, becoming incorporated with it. The bacilli were, however, still capable of growth, so that at a later period, either during incubation, or when the eggs were hatched, they began to multiply, and produced a characteristic brood. It seemed as if the embryonic tissues, without killing the bacilli, exerted an inhibitory effect upon their growth. These results were afterwards extended to the tubercle bacillus; for when bacilli derived from tuberculosis of fowls were introduced into the impregnated egg, they remained latent, without injuring the embryo; but the young chickens, when hatched, became, in many cases, after the usual period of incubation, affected with typical tuberculosis.*

If this, or anything like it, should happen when the tubercle bacillus is enclosed in an impregnated human

* For an account of Maffucci's researches, see Baumgarten's *Jahresbericht über pathogene Mikroorganismen*, 1887, p. 385; 1888, p. 180; 1889, p. 288.

ovum, there might certainly be a hereditary tuberculosis developing after birth. But a period of latency extending till adult life, during which time the tissues inhibit the development of the bacillus, is longer both absolutely and relatively than in the case of the tubercular hen's egg.

Another objection to Baumgarten's theory of the transmission of latent tubercular disease is that the supposed heredity of tubercle is not always direct from parent to offspring. A sort of consanguineous tendency, that is, the occurrence of the disease in uncles, aunts, or grandparents, or even the mere fact of its occurrence in collateral relatives, being generally held to show a hereditary diathesis even when the parents were free from the disease. In all these cases (which are more numerous than those of direct parental transmission) we must go back to the grandparents to find the direct line of inheritance. Baumgarten supposes that the period of latency is here extended over two generations, that is to say, a tubercular parent transmits latent bacilli or their spores to his *grandchildren* passing through the body of the *children*, who are unaffected. This is to make a large demand upon the scientific imagination. We must suppose, for instance, that the female child of a phthisical parent may be born with bacilli or their spores lodged in the ova of her immature ovaries, though, perhaps, in no other part of her body; and these bacilli only develop when the ovum is impregnated, and born as a separate individual. The chief evidence to support this hypothesis is the alleged occurrence in the bodies of the children of tuberculous parents, for instance, in lymphatic glands, or other situations, of small masses of latent tubercle which may be discovered *post mortem*, never having undergone further development during life. With respect to this we must say that very minute and critical sifting of the facts is required.

I have presented this doctrine of direct hereditary transmission of the tubercle bacillus, as it is stated by its supporters, because, though by no means proved, it seems to be the only alternative or supplement to the theory of contagion, in explaining the continued existence of the bacillus as a parasite, and the consequent endemic continuance of tubercular disease.

It certainly seems to explain better than any other hypothesis the rare occurrence of fœtal tuberculosis, and possibly a good deal of the tubercular disease in early life. But to regard it, with Baumgarten, as the main factor accounting for tuberculosis in adults, seems to me an

exaggerated way of looking at the question. Other facts which make against this explanation are the liability to phthisis of foreign races of mankind (*e.g.*, negroes) and wild animals kept in confinement, when they are brought into a tuberculous population such as that of England.*

TUBERCULOSIS FROM DOMESTIC ANIMALS.

There still remains one possible factor in the continuance and preservation of tubercular disease in human societies, that is, its communication from domestic animals, especially from horned cattle. Great importance has been attached to this relation. It has been supposed that tubercle was originally a bovine disease which has been transmitted to man, and that its existence in our domestic breeds of cattle is responsible for a good deal of human tuberculosis. About its prevalence in cattle there can be no doubt; nor that it is propagated by the two means of contagion and inheritance; so that the bacillus is quite capable of continuing its species in the bovine race without living in any other medium, animated or inorganic. These facts have been clearly established by the observations of skilled veterinarians. The question for us is whether the bovine disease is transmitted to man.

If transmitted, it can hardly be in any other way than by the use as food of products derived from these animals, that is, of meat or milk. There can be little doubt that transmission of tubercle by these means is at least possible, and there is some evidence as to its probability, but the problem is a very complicated one. I do not propose to discuss it now, since the question is still under the consideration of the Royal Commission on Tuberculosis, of which I am a member; and it would be premature to express any individual opinion upon it. But no one can suppose that this is the principal means by which the disease is kept alive among men. If we had no milch cows, and ate no beef, we should still have tuberculosis; as may be seen by the example of countries like Japan, where milk is hardly used as an article of diet, and beef very little, while tubercular disease is far from uncommon. It cannot therefore be at most more than a contributory cause.

One curious question as regards animal tuberculosis

* For Baumgarten's views see his *Lehrbuch der pathologischen Mykologie*, vol. ii, p. 626 *et seq.*

is this: If domestic animals give us tubercle, is it not also possible that we may convey it to them? Is not a phthisical cowman or dairymaid a source of danger to the animals under his or her care, especially when they are shut up in stalls?

The same possibility applies in an eminent degree to another class of animals, namely, to wild animals kept in menageries. There is no reason, I think, to believe that in their native haunts they suffer from tuberculosis, yet we find that a large number of the animals dying in the Zoological Gardens die of consumption. It cannot be hereditary in their case (and this might be taken into account in weighing the influence of heredity in producing tubercle), nor can we believe that clay soil, dampness, confinement, and so forth, are more than contributory causes. The infection must come from some source in the country which these creatures have unwillingly adopted as their own. Is it our phthisical population, or is it an infection of their cages, which conveys to them the fatal bacilli? This question might be, in the interests of zoology, well worth consideration.

Conclusion.

Considering, finally, what is it that constitutes tuberculosis an endemic disease, and maintains its existence, I conclude that this is due to the continued existence in the country of a specific organism, the tubercle bacillus.

That this organism has no proper home in external nature. It remains to be proved that it ever lives, develops, and multiplies outside the body of some animals. So far as our present evidence goes, it is a true parasite, and carries on its parasitic existence predominantly in men and bovines.

Hence tuberculosis is not a soil disease; its existence and diffusion are connected with human societies; still, it may keep alive in human dwellings for a time as yet undetermined.

The influence of external circumstances on the prevalence of the disease is undoubted, and this question is of the highest practical importance; but such circumstances are not the determining cause of the disease.

The continuance of the species bacillus tuberculosis as a human parasite is secured by its transmission in two ways: by passage from one host to another, that is, by

contagion direct or indirect; and by inheritance. The former of these methods is probably by far the most important, transmission by heredity being subordinate. Nevertheless, opinions still differ, and will perhaps always differ, as to the relative importance of these two factors.

The parasitism of the bacillus in bovine animals is quite independent of its human parasitism, but may contribute to the latter. The actual importance, however, of this factor in keeping up human tubercular disease is probably small.

The question, What conditions of weakness or vigour favour or resist the invasion of the human organism by the parasite? is an entirely different one, though its importance cannot be denied. Any conclusions which may be arrived at as to the immunity or predisposition of particular races or individuals will not affect the laws governing the distribution and transmission of the parasitic micro-organism.

In conclusion, gentlemen, I hope that I have shown sufficient reasons for regarding tuberculosis as a specific endemic disease, and therefore belonging to that class of diseases with which the Epidemiological Society has always concerned itself.

MEASLES EPIDEMICS, MAJOR AND MINOR.

By B. ARTHUR WHITELEGGE, M.D.,
County Medical Officer, West Riding, Yorkshire.

(*Read: Dec. 21st*, 1892.)

Among the principal zymotic diseases of this country, two are made conspicuous by certain rather remarkable negative characters. We have learned little or nothing of their bacteriology, of any vaccine or attenuated virus, of any relation to lower animals, of any tendency to endemic localisation, or power of living in the soil, or of any possibility of diffusion by means of water, or milk, or other food. As regards nearly all the other epidemic diseases, new facts are constantly coming to light, and, with advancing knowledge, have come better means of prevention; but measles and whooping-cough have, as yet, shown little tendency to diminish their ravages.

I have selected one of these two—measles—as the subject of my paper, not with any hope of throwing new light upon the dark places in its etiology, but to try and show from the statistical side that there is often more order and system in its epidemic fluctuations than is generally recognised, a point which has a bearing upon the burning question of notification of measles.

In bringing this subject once more before the Epidemiological Society, I am following a well-beaten track, and I shall have occasion more than once to refer to the excellent papers contributed by Dr. Campbell Munro in 1891, and by Dr. Arthur Ransome in 1882.

All authorities are agreed that measles is a highly infectious disease, dependent (so far as we know) for its very existence upon transmission from one human being to another, with or without the intervention of *fomites*. Every year or two, in towns, and even in rural districts, it becomes epidemic for a few weeks or months, and then subsides again, leaving the population, as a whole, less susceptible than before, and the actual sufferers usually free from risk of further attack. Many causes are concerned in the production of these familiar brief epidemics. First, of course, the presence of the measles virus in the district.

Practically, this means the presence of cases of measles, for it is evident that the enormous mass of infective material cast off during an outbreak speedily becomes inert, or the epidemiology would be very different. Very possibly it may for a time entirely disappear from country districts or small towns, and Prof. Hirsch shows that, in insular communities like Iceland and Faröe, epidemics occur at long intervals, and only when infection is reimported. But it seems that the apparently complete cessation between epidemics in large English towns is often due simply to the fact that deaths only are recorded. When attacks are notified, the continuity is practically unbroken; such, at least, is the inference suggested by the notification records of Edinburgh, Birkenhead, and Rotherham.

Secondly, the accumulation of susceptible children, a point upon which Dr. Ransome rightly lays great stress. This contributory cause is as constant in its action as the birth-rate itself. How far the accumulation must go before an outbreak occurs is a wide question, the answer to which depends partially upon local conditions and accidents.

Among the conditions tending to shorten the interval between successive epidemics are density of population, facility for close contact between infected and uninfected children at school and elsewhere, and certain meteorological states. It would be lengthened by the converse conditions —sparsity of population, scanty intercommunication, especially among children, precautions as to isolation, and unfavourable states of weather. In some means, also, the degree to which the previous epidemic extended will affect the question of recurrence. If the last outbreak completed the exhaustion of the susceptible, by attacking all who were capable of infection, then the accumulation has to begin *de novo;* but if, as far more often happens, the exhaustion is only partial, the epidemic being arrested by hostile influences (of weather or isolation, for example), then the requisite degree of accumulation will soon be reached. And, further than this, the degree of accumulation which is sufficient is a variable quantity, dependent upon the other conditions prevailing at the time. It is no uncommon experience to find a threatening prevalence of measles subside without attaining its due and usual proportions; possibly to reappear after a few weeks or months of absence.

Then, again, the conditions may be such that no definite explosion occurs, but there is a protracted prevalence, extending much beyond the usual limits of time and exhaust-

ing the susceptible population very slowly and imperfectly. The spread of an epidemic of measles through the various quarters of a large town is by no means always rapid. Here, for example, is a table given by Dr. Spottiswoode Cameron

MEASLES—LEEDS—1890-91.

Monthly Death-rates in Registration Sub-Districts per 10,000 living.

	July.	Aug.	Sept.	Oct.	Nov.	Dec.	Jan.	Feb.	Mar.	Apr.	May.	June	Year.
North ..	—	4	2	—	2	10	58	37	79	43	7	—	20
West	—	3	2	1	8	4	3	3	13	16	2	1	5
South ..	—	4	—	3	—	6	16	55	47	24	27	31	18
Henslet ...	2	2	7	7	23	11	5	2	4	2	2	—	5
Holbeck ...	—	—	—	—	6	13	17	17	—	6	—	9	5
Wortley ...	—	—	—	2	3	13	21	—	11	11	3	2	5
Kirkstall ...	—	—	—	—	9	11	4	4	14	4	4	—	4
Bramley ...	—	—	27	21	124	21	—	9	—	—	—	7	17
Chapel Town	—	—	—	—	—	—	—	19	15	—	—	—	3
Whitkirk ...	—	—	—	—	—	—	—	—	—	—	—	—	—
BOROUGH	—	2	3	3	12	9	17	15	24	15	5	4	9

in a report upon the epidemic of measles in Leeds in 1890-91. It shows the mortality for each registration sub-district and for each month separately, the rates being in all cases annual rates. The lowest line shows that the maximum for the borough occurred in March, but that the rise was by no means unbroken. The last column brings out clearly the unequal distribution of the epidemic in the different districts, while the body of the table shows equally plainly the irregularity in point of time. Not only did the several districts suffer at very different periods, but there are examples (*e.g.*, Holbeck and Bramley) of the same district being re-attacked a few months or weeks after the maximum mortality had been reached. The maximum mortality was recorded in Bramley and Hunslet registration sub-districts in November, while in South Leeds it was delayed until February, in North Leeds until March, and in West Leeds until April. In West Leeds, however, there had been a previous and smaller maximum in November. Cameron points out that two districts somewhat similar in their semi-rural character, viz., Kirkstall and Bramley, had very different experiences in this outbreak: the former suffered comparatively slightly, but from November to May, with a maximum in March; while Bramley was attacked far more severely, but for a shorter period—September to December. It recurred, however, in February, and again in June, showing that the susceptible population was not exhausted.

Clearly the extension from district to district was far from being explosively sudden, nor could the exhaustion of susceptible population have been at all complete. I have found the same in measles epidemics in Nottingham, and I have no doubt that it is in accord with general experience. In large towns, measles epidemics, especially those of low intensity, often wander about in a somewhat flickering fashion, according to the balance between many conflicting influences.

Now I come to a third point. Assuming that measles is present in a town, as it nearly always is, and that reaccumulation of susceptible persons goes on, as it always does, so that an outbreak sooner or later is inevitable—at what time of year are the climatic conditions most favourable for the spread of the disease in epidemic fashion? In London there are two such periods, very dissimilar in temperature, namely, June and December.

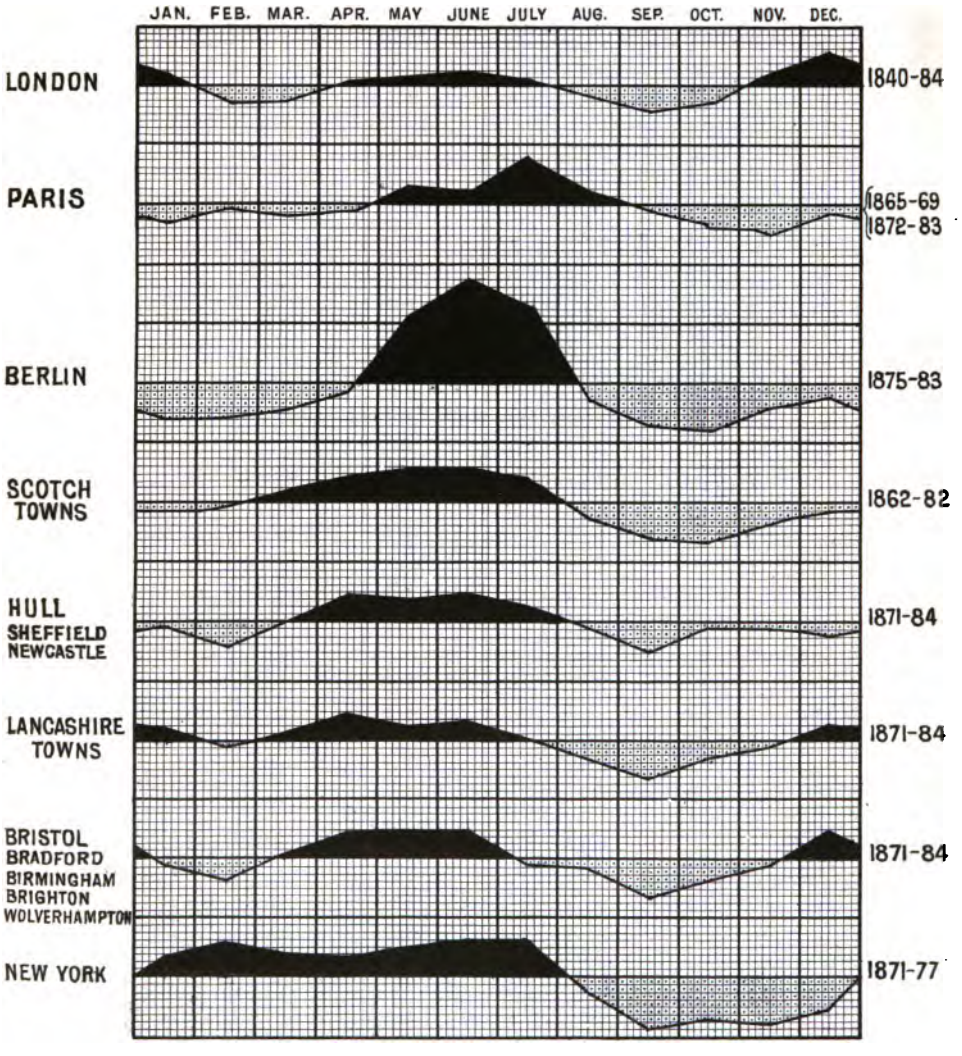
The Registrar-General, in his Annual Report for 1884, shows that the double maximum is by no means general, and that the winter maximum, which in London and Lancashire is greater than the other, is less prominent in other towns, and in many cases (Hull, Sheffield, and Newcastle, for example) is scarcely perceptible (Fig. 1). He suggests that "where the measles mortality in a town is habitually high, there are in it two measles seasons—a summer and a winter season; and that when the measles mortality is habitually low, the winter prevalence is either absent or comparatively slight."

On this side of the Atlantic the winter maximum seems to be pretty constant to December, though in New York it is delayed until February. The spring or summer maximum is more variable. As a rule, the course is highest in May and June, but in Edinburgh and some English towns the actual crest is reached as early as April, while in Paris and New York it is as late as July.

It seems reasonable to anticipate that in countries where the climatic variations are of more orderly and typical character than in this foggy island, and also of wider range, the seasonal curve of measles would be more intense; that is, that the maximum would be higher and the minimum lower. The curves for Berlin and New York are not opposed to this view.

All these are of course curves of mortality. The attack-curves for Birkenhead and Edinburgh are the only two which I have obtained, the former being based upon figures which Mr. Vacher has kindly given me, and the

Fig. 1.



MEASLES, —— MONTHLY DEATHS.

Calculated as percentages of the monthly average. (Buchan & Mitchell's Method)

The first seven curves are based upon figures given in the Annual Report of the Registrar General for 1884, page XV.

The last is roughly copied from Buchan & Mitchell. Journ. of the Scottish Meteorological Society 1878, page 174.

Groups 5 & 7 were selected as having a low Measles death-rate, while group 6 resemble London in having a high rate.

latter upon Dr. Harvey Littlejohn's researches.* At Edinburgh the attack-curve in spring is seen to reach its maximum in March and April, a month earlier than the death-curve, and the reason for the difference is obvious; but the smaller winter maximum of attacks, as well as deaths, falls in December. At Birkenhead the winter maximum is the greater of the two, and reaches its height in December; the smaller summer maximum has its crest in June.

Dr. Spottiswoode Cameron has observed that certain meteorological conditions are often coincident with, or immediately precede, rapid outbreaks of measles. These are high barometer, dryness, increased diathermancy, and diminished rainfall. He makes special note of this occurrence in connection with the Leeds epidemic of 1891; and the observation is in harmony with the fact that the phenomenally dry year, 1887, was one of high mortality from measles in the country generally.

Dr. Ballard† has expressed the opinion that measles epidemics are checked by rise of temperature above 60° F., or by a fall below 42° F. Dr. Ransome and Dr. Munro suggest that climatic conditions are operative by establishing a *locus minoris resistentiæ*, but Hirsch is opposed to this view, although he states (not quite correctly, I think) that "it is everywhere the cold season in which epidemics of measles most commonly begin, and in which they are apt to spread farthest". It is a general opinion among medical men that the winter mortality from measles is largely dependent upon wintry weather; but although this may account for a higher case mortality, it scarcely explains the prior fact of winter *prevalence*, and still less the even more constant prevalence in spring or early summer.

To sum up once more, we have in an ordinary town measles always present and ready to spread, susceptible children always accumulating and getting nearer and nearer to the degree of density requisite for epidemic extension, and, thirdly, climatic influences, which from time to time (usually once, but sometimes twice a year) afford in some way maximum facilities for the outbreak.

Assuming the multifarious conditions in question to be tolerably uniform, at what intervals of time will reaccumulation bring about an outbreak of measles? In England, about every two years usually. There are many exceptions, but not so many as a casual glance at the annual

* *Ten Years' Compulsory Notification of Infectious Diseases in Edinburgh*, 1890.

† *Eleventh Report of the Medical Officer to the Privy Council* 1868.

records would indicate. The Nottingham quarterly rates (Fig. 2) indicate a very marked rise every second winter, from 1877 to 1889. Each year had its share of an epidemic, at either the beginning or the end, and hence the yearly figures yielded no definite course, nor any clear indication of the epidemics which nevertheless occurred. Before 1877, and after 1889, this rhythm is not observable.

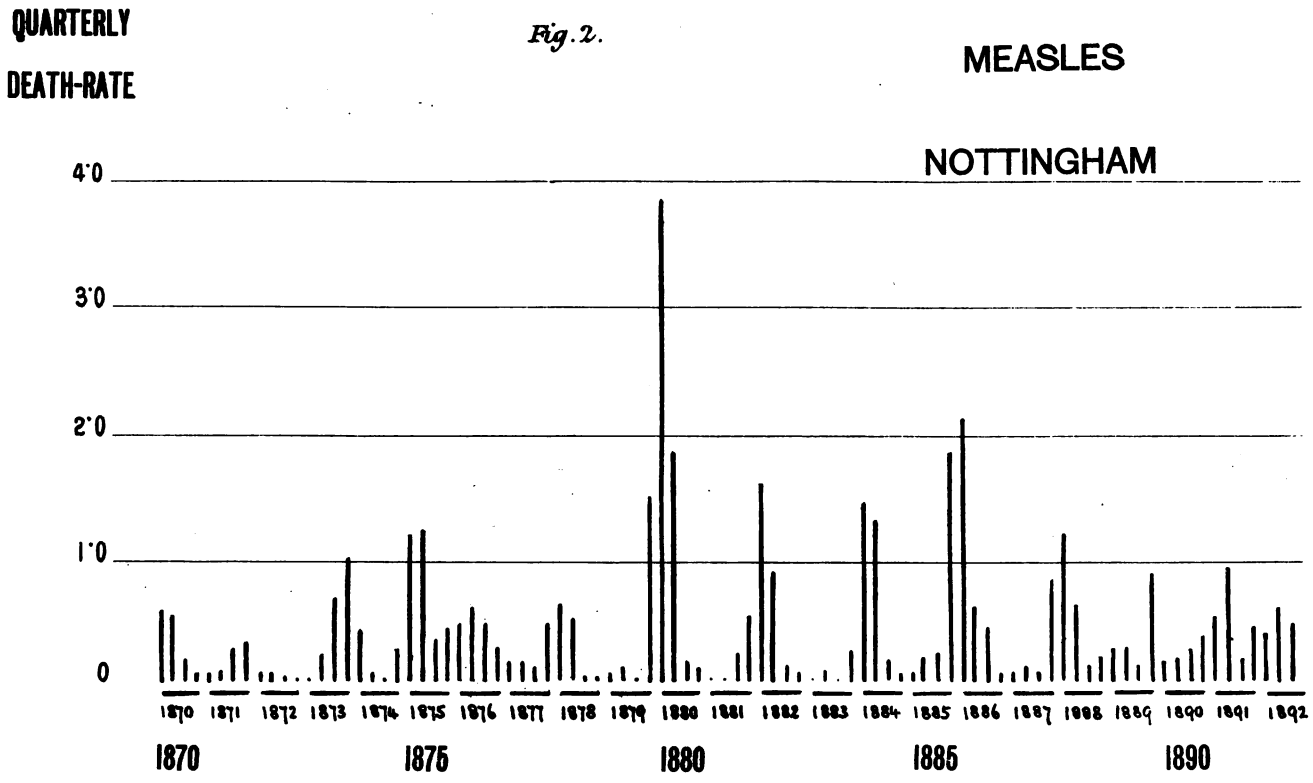
The Edinburgh figures (Fig. 3), for which I am indebted to Dr. Harvey Littlejohn, show very clearly the complete way in which annual totals may obscure the real periodicity of epidemic recurrence. The quarterly curve of notifications proves that the usual biennial average prevails in Edinburgh. The annual curve of cases or deaths would raise no suspicion of this, but would point rather to an average interval of three or four years. The explanation is of course obvious. Three of the seven epidemics occurred in winter, and each was counted in the records of two consecutive years, part in each; hence the comparison of these two years can tell little or nothing of the occurrence of the epidemic.

Dr. Munro states—and I can fully bear out his statement—that the two-year interval is to be found in many town records. Nevertheless, it is by no means constant or invariable, nor does regularity in the past ensure continuance in the future. In Nottingham it was scarcely perceptible before 1877; in London and Liverpool every year brings more or less epidemic prevalence; in Edinburgh the interval varied from eighteen to twenty-five months, and averages twenty months, as Dr. Harvey Littlejohn points out. At Bolton an eighteen-months' interval was fairly constant from 1884 to 1891, but it was preceded by an interval of nearly three years, and the outbreak due in the early part of 1892 failed to make its appearance. Rotherham has had epidemics during the last ten years, at intervals of three, two, two-and-a-half, and one-and-a-half years. Later on we shall meet with many similar examples. Hirsch gives instances of three, four, five, and six-year intervals. Ransome has shown that in Sweden the interval is usually five or six years, and this seems to be true for Norway also.

So far as English towns are concerned, Hirsch's dictum,* that recurrence "depends *solely* upon two factors, the time of importation of the morbid poison, and the number of

* *Geographical and Historical Pathology*, vol. i, p. 161.

Fig. 2.


QUARTERLY
DEATH-RATE
MEASLES
NOTTINGHAM
4·0
3·0
2·0
1·0
0
1870 1871 1872 1873 1874 1875 1876 1877 1878 1879 1880 1881 1882 1883 1884 1885 1886 1887 1888 1889 1890 1891 1892
1870
1875
1880
1885
1890

persons susceptible of it", cannot be accepted in its entirety. There are other influences at work. Even in the Faröe Islands, where, as he tells us, only four epidemics have been recorded, in 1781, 1846, 1862, and 1875 respectively, one of these (that of 1862) was slighter than the rest.

What is true in this proposition is embodied in Ransome's view—that epidemics of measles can only arise "when the proximity between susceptible persons becomes sufficiently close for the infection to pass freely from the one to the other".

So far I have spoken only of the *quantity* of measles, and have followed Hirsch, Ransome, and Munro in representing the epidemic outbursts as mechanical, differing, however, from Hirsch in recognising a complexity of variable controlling condition. My chief object to-night is to show that there are occasional definite variations in its *quality* which play an important part in determining its epidemic character. It is of course a matter of common observation that some epidemics of measles are so mild in type as to cause few, if any, deaths, while others kill ten per cent., or more, of those attacked. The latter type is not familiar in this country, although I shall have to mention in detail one or two which were unusually malignant in character.

As a rule, the character, whether mild or otherwise, is maintained throughout the epidemic, and, indeed, in successive epidemics in the same locality. It is true that occasionally we find the earlier or later part of an outbreak differing from the rest in fatality, owing to the supervention of pneumonia, which we may suspect to be due to climatic conditions, or possibly to the addition of another zymotic element. Still, these abrupt changes are exceptional, and I think it will accord with the experience of most of us, if I say that although measles may assume a very mild or a very malignant type, it does not readily or suddenly pass from one type to the other, save under exceptional conditions.

The occasional change of type did not escape Dr. Ransome's notice, and he offered the suggestion that the virulent cases which are sometimes observed at the beginning of an epidemic may be due to intensification of virus by transmission through susceptible persons, in such manner as to become capable of infecting the less susceptible. A similar phenomenon is now familiar in experimental work upon lower animals in certain diseases, but not yet in measles; and, for my own part, I am inclined to doubt the

safety of trusting to analogy in the present instance. Again, the sporadic cases which bridge over the interval between epidemics may, with equal probability, be supposed to afford examples of special susceptibility, which, nevertheless, have failed to light up an epidemic. Many extensive epidemics, too, are of mild type throughout, from first to last, a fact which in itself negatives the suggestion that multiplicity of cases is a cause of severity of type. The proposition would probably be nearer the truth if reversed.

The measles pestilence in Fiji, which killed off one-fifth or one-quarter of the population in little more than three months, was described in a paper which Dr. Squire contributed to this Society some years ago. The case-mortality was very high, and, measured in this way, the type was malignant; but it seems that where proper attention was paid to the sick, the loss of life was greatly reduced. A writer in *The Lancet* (June 19, 1875) traces the Fiji epidemic to one which prevailed in South Africa in 1872, spreading to Mauritius in 1873-4, South Australia in 1874, and thence to Fiji early in 1875. The disease had been previously unknown in Mauritius, as in Fiji, and at Port Louis 9 per 1,000 of the inhabitants died in three months. In South Australia, again, there had been no outbreak of measles for nearly a generation; and it is specially mentioned that adults suffered in large numbers in Fiji, South Australia, and Mauritius. At Port Louis even advanced ages were not spared.

The accepted explanation as regards Fiji is, that the population were not only unprotected by previous measles epidemics, but had not even such protection as would be derived from the killing off in former generations of those most susceptible. Clear as the evidence of sudden increase of virulence appears at first sight to be, it is not free from ambiguity. There was, according to *The Lancet* account, evidence of considerable severity of type long before the epidemic reached Fiji.

That it would attack enormous numbers, including adults, was only to be expected, seeing that all were unprotected. The principal evidence of malignancy, therefore, seems to be the case-mortality, and that is alleged to have been only high where neglect and exposure prevailed. If we may argue from small-pox to measles, greater susceptibility will in itself account for severity of attack. To put it mathematically, the severity will vary directly as the virulence, and inversely as the resistance—resistance being,

of course, insusceptibility. It is difficult to say how far, after making these allowances, we have to recognise in the Fiji epidemic any special intensification of the measles poison. The same questions arise in connection with the malignant epidemics which Hirsch* mentions among the Indians of the Amazon in 1749, the Hudson's Bay Indians in 1846, the Hottentots in 1852, and the Tasmanians in 1854 and 1861.

In other instances, the exceptional conditions were limited pretty clearly to the privations of war, there being no reason to suppose that previous epidemics had been wanting. Under such circumstances, measles has appeared among bodies of troops, and has sometimes proved very fatal. Hirsch tells us that there was an epidemic among Confederate troops in 1866, resembling ordinary measles in adults, except where aggravated by the effects of crowd, poisoning, or other depressing influences; but in two hospitals the case-mortality reached 20 per cent. He cites other examples of fatal measles epidemics: among French troops during the siege of Paris, and also after the Italian war, and among Paraguayan forces fighting against Brazil. But it is noteworthy that in all these instances of high mortality there was something akin to neglect or exposure; and, as regards the Paraguayans, it is expressly stated that, among fifty men that were properly cared for, there were no deaths. As Hirsch points out, the malignant character was largely, if not entirely, due to accessory circumstances, and not necessarily to any special quality of measles.

In a less degree, the experience of ordinary civil practice confirms this. The proportion of deaths to attacks is far less among the wealthy classes than among the poor or even the artizan class. Thus, at Sunderland, in 1885, measles was most fatal in the districts in which those most affected by bad trade and strikes resided; and at Barnsley, in 1891, the deaths were almost confined to children attending public elementary schools, although numbers of others were attacked.

In ordinary English communities, where measles breaks out every two or three years, these exceptional conditions of general susceptibility and lowered vitality scarcely affect the comparison of one epidemic with another. Each recurring outbreak finds the same sort of population as the last, and the social conditions and average susceptibility are probably not very different.

* *Geographical and Historical Pathology*, i, 167.

If, therefore, we find a change in the quality of the epidemic, without any obvious change in the character of the attendant circumstances, we have to consider whether there is not a difference in the type of measles.

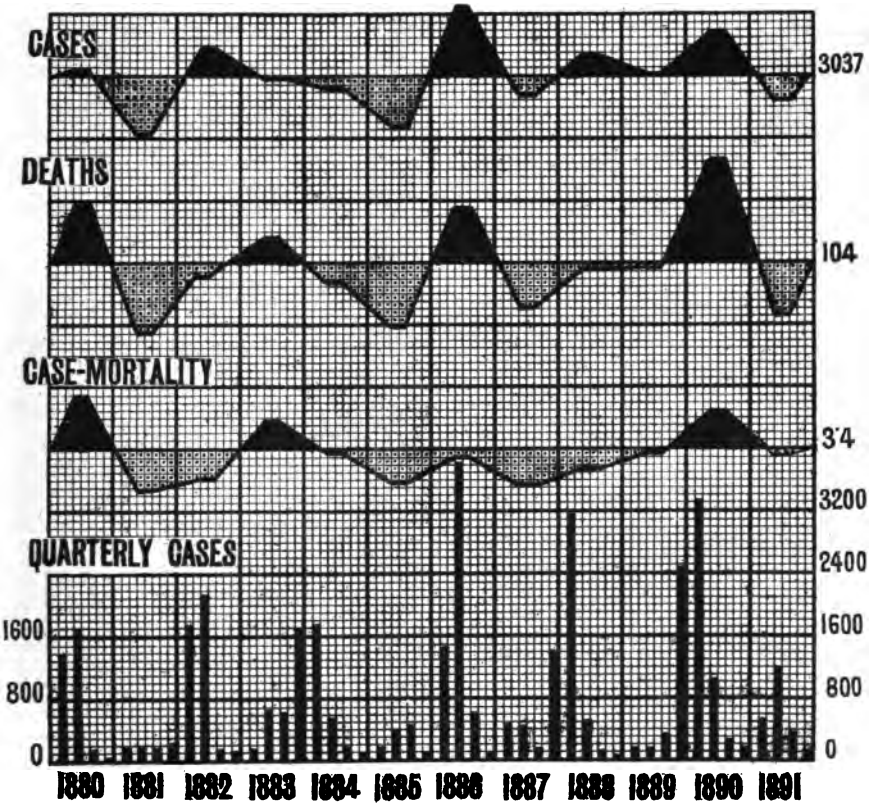
At the outset of this inquiry it would be interesting to know whether the minor outbursts of measles, biennial or otherwise, are attended with any change in the type of disease. Dr. Thorne Thorne has taught us that, in diphtheria at all events, malignancy may increase rapidly during a brief epidemic. I believe, upon grounds which I must not pause to explain now, that the seasonal increase in the prevalence of small-pox, scarlet fever, and enteric fever is, on the contrary, attended with lessened average severity, as tested by case-mortality. As regards measles, I think, but cannot prove, that there is, at all events, usually no increase of severity. The data at my disposal are insufficient to settle the point either way.

If we look to the records of each outbreak separately, the Edinburgh chart (Fig. 3) is, at first sight, strongly suggestive of complete parallelism between the rise and fall of epidemic prevalence, and the severity of type. The annual death-curve and severity-curve are, indeed, quite parallel. But we have already seen that the former is fallacious, and the same reasoning applies to the latter also, in some degree. When an epidemic occurs in winter (1889-90, for example), the deaths recorded in the new year will include not only the fatal cases beginning in that year, but also many which began before December 31st, and are counted among the attacks in the old year's record. Hence the case-mortality will be unduly high in the second year, and unduly low in the first. Were the cases distributed tolerably equally over the year, the error would be small, but they are often clustered in the few weeks before and after Christmas. We can only look for a fair statement of case-mortality where the epidemic begins and ends within a single year, as it did in 1882, 1886, and 1891. In each of these years the mean case-mortality was below the average, and we may fairly conclude that there was no marked increase of severity in those three epidemics, although in 1886 the case-mortality was certainly higher than in 1885 or 1887.

The apparent increase of case-mortality in 1890 may perhaps be accounted for by transfer of deaths properly belonging to the previous year, and the 1880 excess may not improbably have been due in part to imperfect notification.

The 1883 excess is less easy to explain. The fallacy of

MEASLES *Fig. 3.* **EDINBURGH**



The annual totals of notified cases & deaths, and the case mortality in each year, are shown as percentages of the mean values indicated on the right. Each small division corresponds to ten per cent. above or below the mean.

Fig. 4.

MEASLES, —— LONDON.

PERCENTAGE OF TOTAL DEATHS

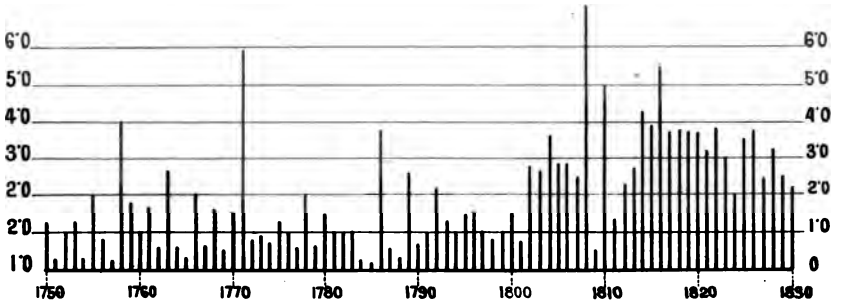
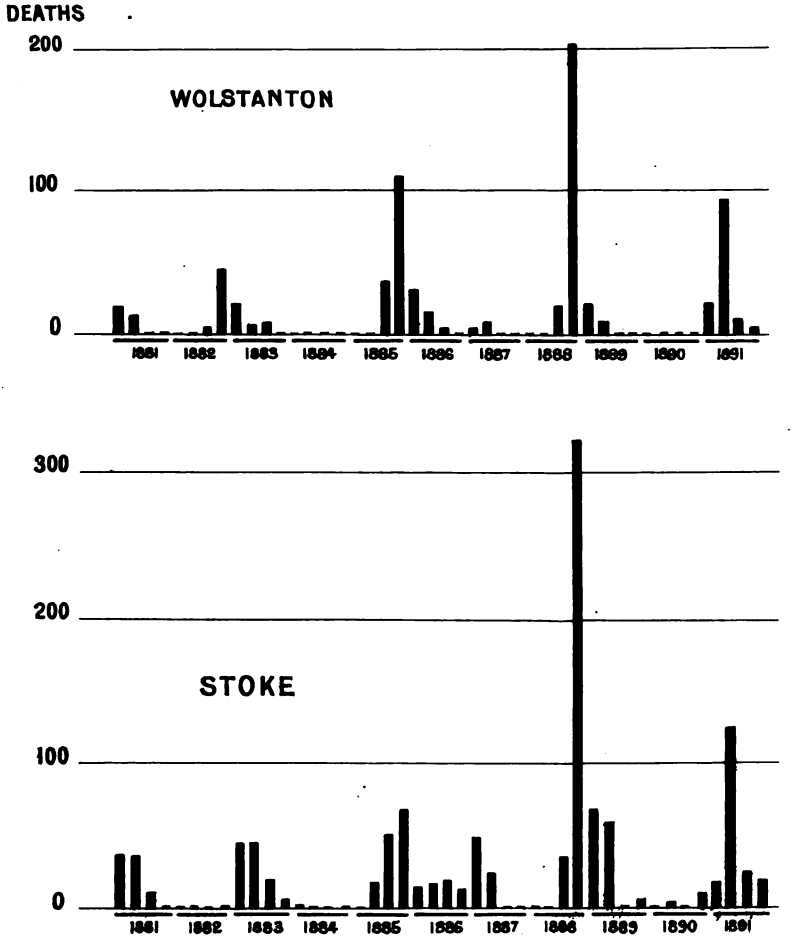


Fig. 8.

MEASLES, —— POTTERIES.



transfer would tend to lower, rather than raise, the apparent case-mortality, since measles was epidemic at the end of the year, and not at the beginning. It seems, therefore, that the prevailing type in 1883 was of rather greater average severity than in the years which immediately preceded or followed, but that there is no proof of corresponding change in the other epidemics of measles during the twelve years.

I have not met with sufficient statistical data from other towns where measles is notified, to enable me to carry this point further.

Now let us look at the records of measles mortality in London for the last century or so. Up to 1830, I can only produce imperfect data, viz., the proportion of measles deaths to total deaths (Fig. 4). Nevertheless, certain familiar points come out clearly, and especially the tendency to biennial recurrence, the alternation of high and low mortality. But there is a further point. Somewhere about the end of the century, the average annual measles mortality began to increase, and seems to have reached a maximum somewhere about 1815, after which it again declined, although in 1830 it was still above the average of fifty years earlier. The gap in the records from 1830 to 1838 prevents us from identifying the point of minimum, but probably it was early in the "thirties", for another maximum (Fig. 5) occurred in the early "forties", and yet another in the "sixties". The "seventies" were comparatively free, but in the "eighties" came another wave, which is, unfortunately, still with us.

To what cause are we to attribute them? Possibly the Elementary Education Act has had something to do with the present protracted rise, but it certainly was not responsible for its precursors.

Accumulation and exhaustion of susceptible units, peculiar meteorological conditions, and the like, cannot account for waves such as these. It is possible, but not probable, that there may have been corresponding climatic, social, or industrial cycles affecting the susceptibility of the population to infection. Time will not permit me to enter into this wide question, but I may mention that I have not yet observed any parallelism in any of the other zymotic diseases, except perhaps diphtheria, although most of them have cycles just as definite as that of measles.

In the absence of any satisfactory theory to account for the phenomena, by cycles of increased susceptibility, or cycles of increased climatic or social facilities for infection,

let us see if there are any facts to warrant the suspicion that the cyclic variation is in the quality of measles itself. Let us suppose for a moment that, from about 1853 onwards, the average character of the disease became more and more virulent year by year. It would then break out as usual every two years. It would kill a larger proportion of those whom it attacked, and, as a further consequence of its greater virulence, it would probably succeed in attacking persons who were proof against the less virulent type which preceded it. Thus the increasing mortality would be accounted for—each successive biennial epidemic attacking a larger proportion of the population than the last, and, moreover, killing a larger proportion of those whom it attacked. After a certain point, say 1863, let us suppose that the conditions were reversed, and that the virulence became less and less each year, so that the declining death-rate would be accounted for by decline in the sickness-rate and case-mortality. This hypothesis has the *primâ facie* merit of harmonising with some of the observed facts, but this alone is not sufficient. I have met with no clinical evidence for or against it as regards London, but among foreign and provincial statistics confirmatory hints are not wanting.

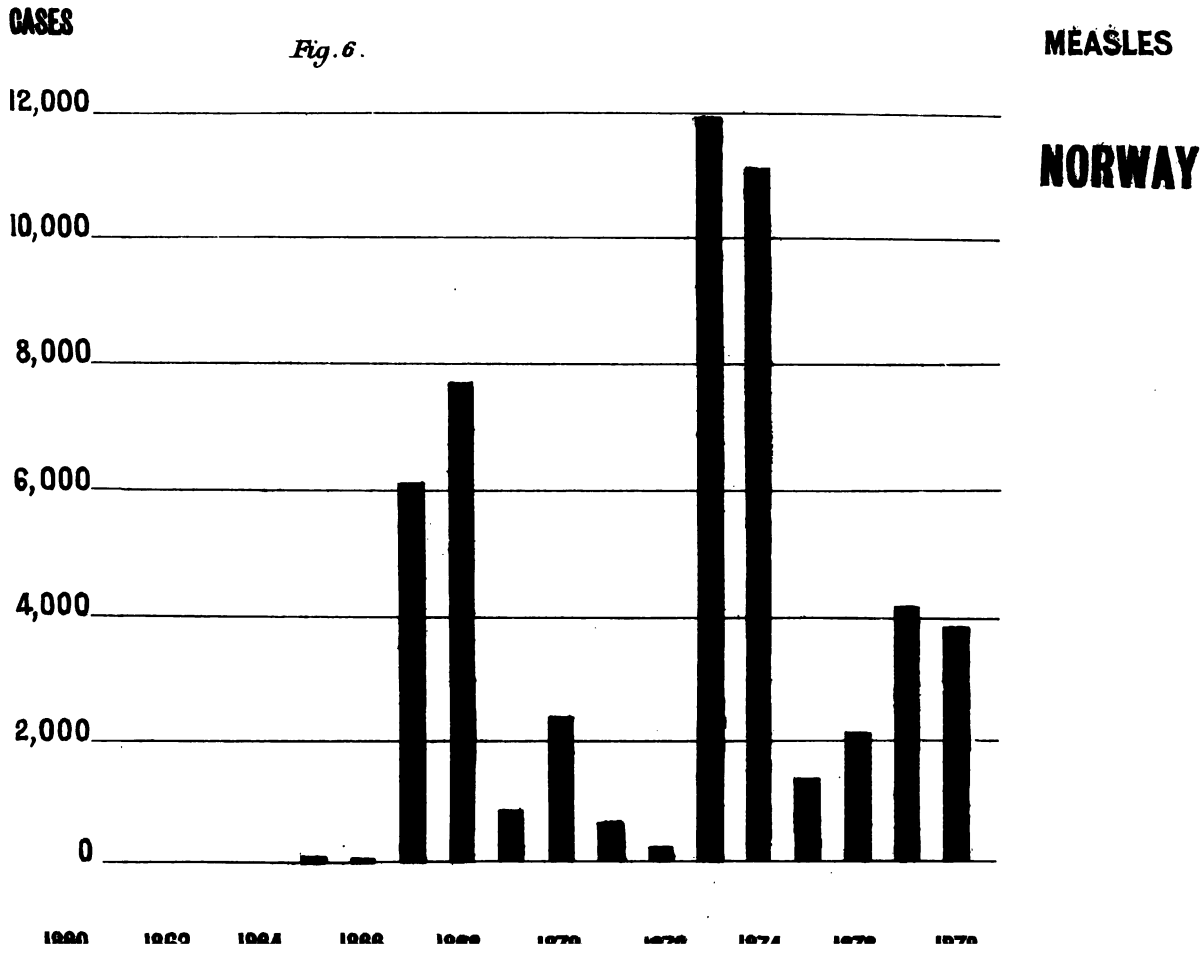
Dr. Ransome* has shown that, in Sweden, measles assumes wide epidemic form every six or seven years, an interval which is intermediate between the two classes of waves which we meet with in England, and which he attributes, no doubt rightly, to the sparsity of population. Whether there is any increase in malignancy during these epidemics in Sweden, anything corresponding to the character which I have suggested as possibly belonging to the twenty-year waves in England, I do not know; but, in the neighbouring kingdom of Norway, the same sort of interval prevails, and there, at least, Johannessen's† records of attacks and deaths (Fig. 6) enable us to recognise a higher case-mortality in epidemic years, during the fourteen years 1865 to 1878. I have no means of gauging the value and accuracy of his statistics, but, so far as they go, they point to a greater malignancy accompanying, and perhaps partially causing, each epidemic recurrence.

Returning to England, the first example which I will take is that of Sunderland. In 1885, measles was rife in

* See *Epid. Soc. Trans.*, 1881-2: "On the Form of the Epidemic Wave and some of its Probable Causes."

† *Die epidemische Verbreitung des Scharlachfiebers in Norwegen.* 1884.

Fig. 6.



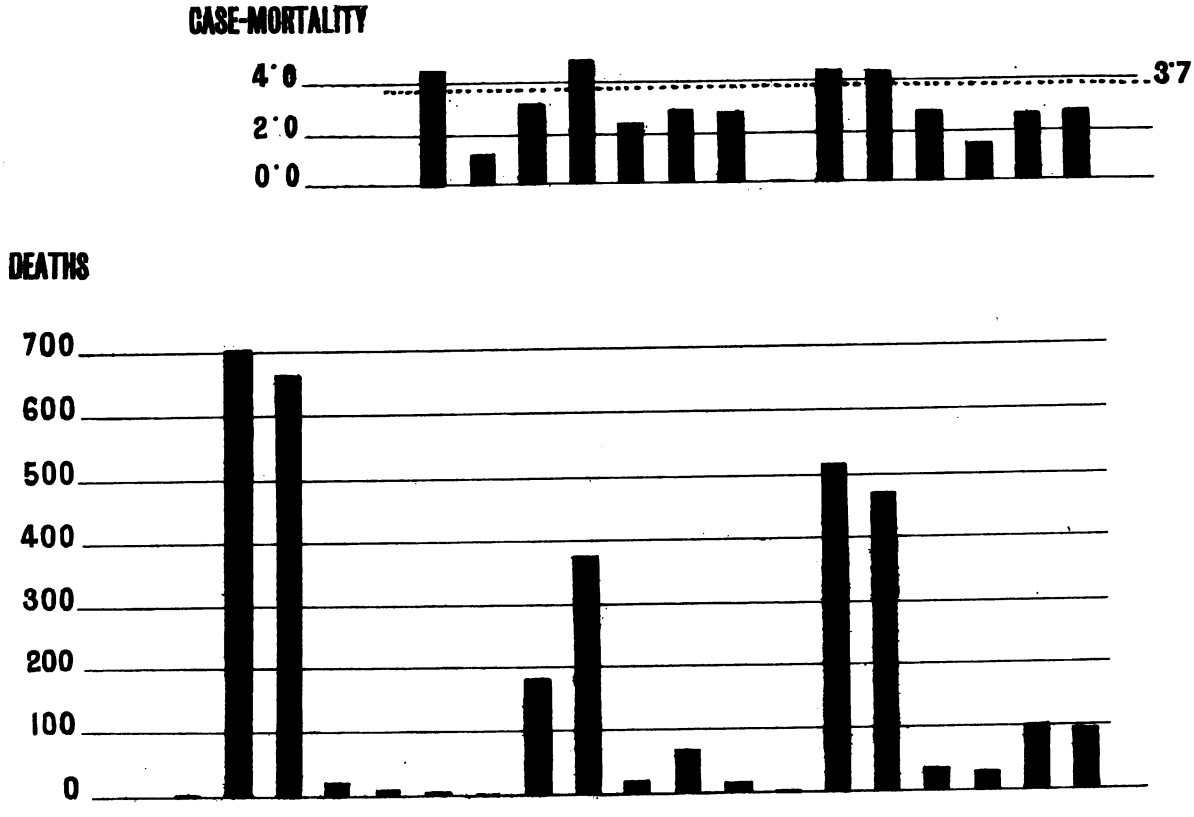
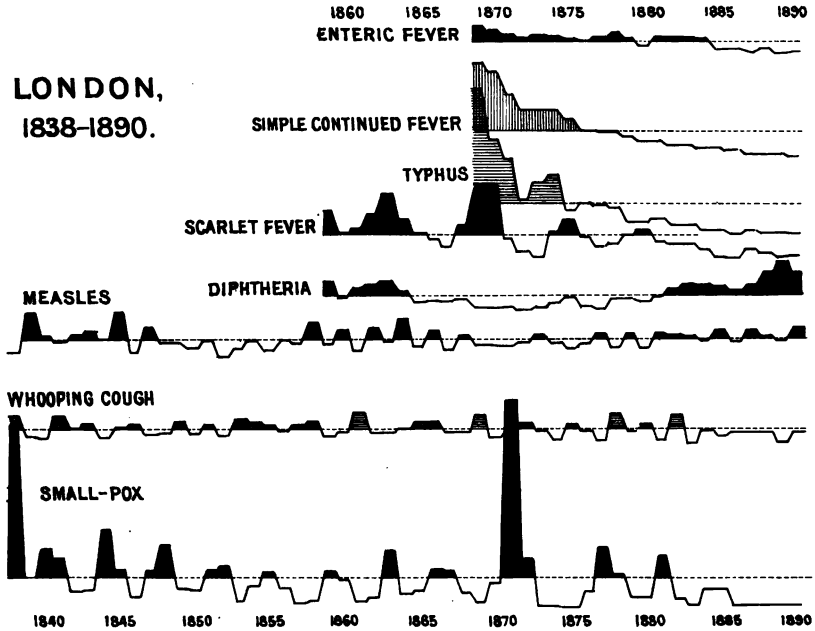

CASE-MORTALITY
4·0
2·0
0·0
3·7
DEATHS
700
600
500
400
300
200
100
0

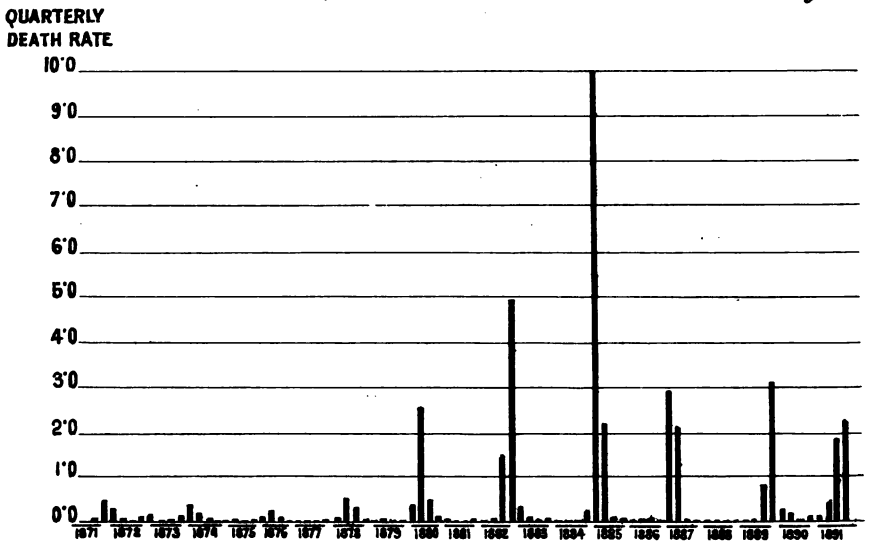
Fig. 5.

FLUCTUATIONS IN DEATH-RATES FROM CERTAIN ZYMOTIC DISEASES.



The curves are constructed upon Buchan and Mitchell's method, showing deviations from the mean as percentages. The scale is the same in each case, but is not shown in the chart.

MEASLES, ——— SUNDERLAND. *Fig. 7.*



that town, and so fatal and widespread as to cause in one quarter a mortality equal to an annual rate of 9.0 per 1,000 from measles alone. Dr. Harris, then Medical Officer of Health for Sunderland, in his Annual Report for 1885, describes the epidemic as one of quite exceptional severity of type. The proportion of deaths to known attacks was 29.1 per cent., and it was his opinion that comparatively few cases were unreported. He gives figures which show a biennial recurrence of measles in previous years, and I have carried these records a few years further in each direction, and given them in quarterly, instead of annual form, with the results shown by the diagram (Fig. 7).

It is scarcely possible to look at the Sunderland chart and doubt that at least some part of the ferocity of the 1885 epidemic was due to causes which can be traced for many years previously. From 1875 onwards, the biennial explosions are tolerably constant in their sequence, and equally constant in the rapid increase of mortality in each successive epidemic. The explanation which I suggest is, that the quality of measles has undergone progressive changes, from a minimum severity in 1875 to a maximum in 1885, subsiding again after 1885; that the biennial explosions were regulated as to quality by the prevailing phase of measles, and as to quantity or extension by the number of persons susceptible, by the meteorological conditions, and by the facilities for infection at school and elsewhere; and that the whole incidence of measles in Sunderland from 1875 to the present time is, in a sense, one great wave or cycle, interrupted repeatedly in a mechanical fashion by the temporary exhaustion of the susceptible, but exhibiting, in spite of these interruptions, a progressive increase in extension and malignancy, culminating in the phenomenal outburst of 1885.

Another example is afforded by the epidemic which raged at Hanley, in the Potteries, in 1889, and was investigated by Mr. Spear. Here, again, we have a wide prevalence of measles, and high mortality; and it is evident from Mr. Spear's report that the symptoms were of aggravated type, and the case-mortality not far short of 9.0 per cent., which, as he says, is enormous for measles, though much below that recorded in Sunderland four years earlier. "The type of the prevailing disease differed only from the normal in presenting some unusual general severity of the ordinary symptoms of measles." According to the view which I have ventured to advance, we should expect to find that

this malignant type did not commence in 1889, but must have had a history to which the Registrar-General's records of measles mortality in former years would afford a clue. Here (Fig. 8) are the quarterly totals of deaths attributed to measles in the two registration districts principally concerned. Again, a succession of outbreaks, at not very regular intervals, but steadily increasing in destructiveness, until in the winter of 1888-9 there came an epidemic conspicuous above the rest by its virulence.*

I have no information as to the clinical characters or case-mortality in the epidemics at Sunderland and Hanley, which preceded the great outbreaks of which description has been given. The third example, though on a smaller scale, is in this respect more complete.

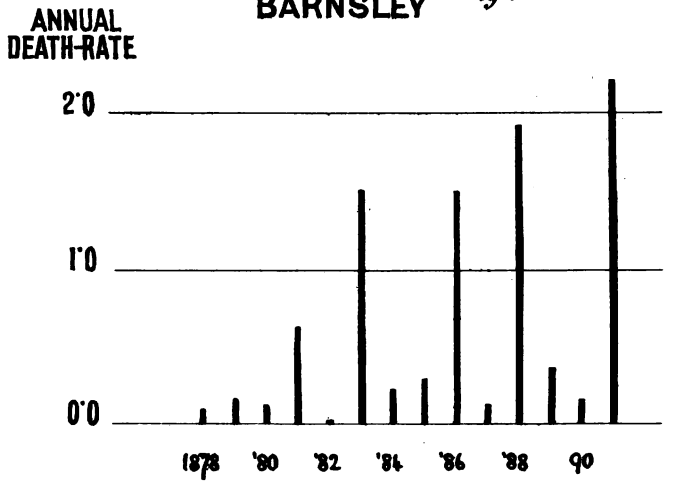
At Barnsley, a Yorkshire town, with some 35,000 inhabitants, measles was epidemic in 1881, 1883, 1886, 1888, and 1891 (Fig. 9). The interval between epidemics was more uniform than the annual figures indicate, and was in each case about two-and-a-half years. Although the mortality from measles in 1891 was 2.2 per 1,000 only, in point of fact $\frac{12}{13}$ of the deaths occurred in the first quarter, and none in the third and fourth, so that the measles death-rate in the first three months was at the rate of 8.0 per 1,000 living.

I have Dr. Sadler's authority for the observation that the epidemic of 1891 was characterised by severity of type, as well as wide extension. Among other instances "of what would appear to be a more than ordinary infectious power", he gives the following, in a special report to the Corporation: "Up to January 1891, the cases had been mainly amongst children of the class who attend public elementary schools; but, on the second of that month, a dance for young people was given in the rooms of a large, airy hotel, attended by above sixty children, educated at home or in private schools. At this dance, a child from a village six miles off was present, who had been medically examined that day, and pronounced to be only suffering from slight catarrh, but who

* Within the last few weeks Dr. George Reid has been kind enough to make enquiries for me among the leading practitioners in the districts chiefly affected as to the character of the outbreak. Their almost unanimous opinion, he tells me, was that the excessive mortality in 1889 was due simply to excessive prevalence; the type was not more severe than in other epidemics! It is difficult to imagine either that Mr. Spear's emphatic statements, made at the time, were unfounded, or that the exceptional severity he describes should be forgotten locally within four years.

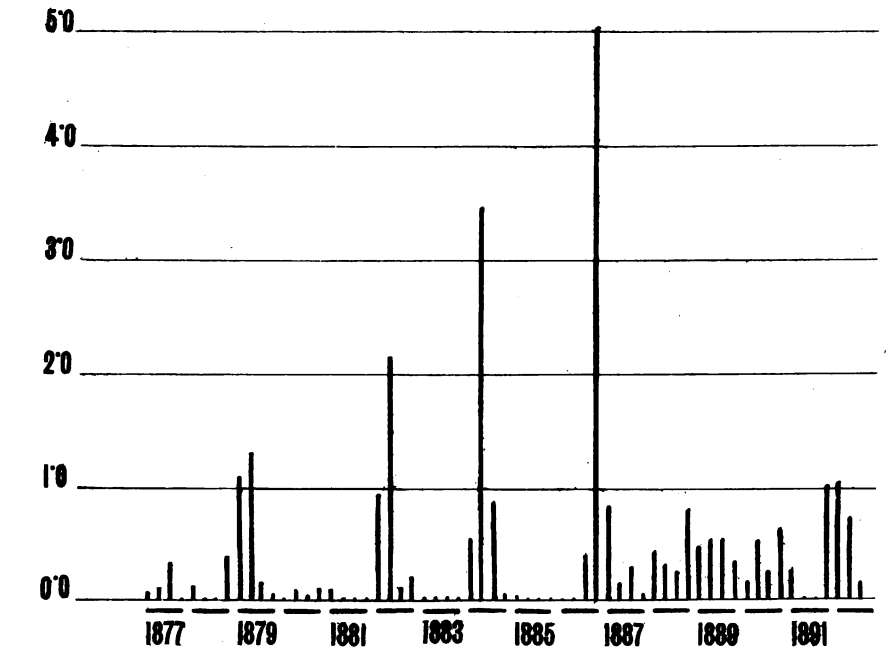
MEASLES

BARNSLEY *Fig. 9.*



MEASLES

WOLVERHAMPTON *Fig. 10.*



next morning proved to have measles. Within a fortnight, twenty-five of the children who were at the dance were ill with measles also; some of them had the complaint very severely." Here, again, we have an outbreak of measles conspicuous for its infectiousness and severity of type, though apparently in a less degree than those at Hanley and Sunderland. If we proceed to inquire what the history of measles in Barnsley had been in previous years, the record is certainly suggestive. I can only give annual figures, but the abruptness with which the "measles years" stand out from the rest shows that quarterly data are scarcely necessary. What was the type of outbreak in 1888 and 1886? Here, fortunately, Dr. Sadler's acumen enables us to establish what at Hanley or Sunderland was only a matter of surmise. The 1888 epidemic was severe in type, less severe than in 1891, but more so than in 1886.

These three examples are the most typical that I have met with. In each case my attention was drawn to them not by heavy mortality merely (for that might be due to long absence of epidemic visitation, or to other conditions), but by the recorded malignancy of average attack. Each of them shows traces of a cycle, corresponding tolerably well in duration with the suggested cycle seen in the London statistics. I have not ascertained whether the records for Sunderland, Hanley, or Barnsley, if traced further back, would reveal other waves of like character. I have examined the mortality statistics of a large number of towns for the years covered by the Registrar-General's quarterly returns, finding therein abundant examples of tolerable regularity in periodic explosions, but very few unmistakable evidences of cyclic changes of the kind now in question. Some indications there certainly are, but, in the absence of any clinical, or even case-mortality data, I should hesitate to class them with the Sunderland group. Manchester, for example, looks as if its cycle might have culminated in 1887. In Derby, it would seem that from 1882 to 1890 the intensity increased, notwithstanding the depressed (and therefore protracted?) wave of 1885. Bristol has a recent record which is suggestive of a sharp outbreak this winter, if average climatic conditions prevail. Wolverhampton, again (Fig. 10), had a series of epidemics of larger and larger mortality, until the winter of 1886-7; then the conditions seemed to have changed, and the measles wave becomes more continuous and less explosive.

At Stockholm the increase is still more striking, but the complete absence of the outbreak due in 1889 would naturally add to the magnitude of 1891 epidemic.

The longer interval which Dr. Ransome showed to prevail in Sweden as a whole, up to 1870, is not to be found in Stockholm since 1881—a fact readily explained in accordance with his views, by the density of population.

The Newcastle chart recalls that of Sunderland, but Dr. Armstrong tells me that he has no recollection of any special malignancy of type in the widespread epidemic of 1885.

The Jarrow chart, which will be found in Dr. Munro's paper,* shows some indication of a long interrupted wave of the cyclic kind. Dr. Munro thinks, and gives good reason for thinking, that the admirable system of supervision of schools, which was instituted by him, kept the 1889 epidemic to comparatively small limits; but, if we look to the previous epidemics of 1887, 1885, and 1883, we see that each successive wave was lower than its predecessor, and not merely that of 1889. Before 1883, there are indications of gradually increasing severity in successive outbreaks. It seems not unlikely, therefore, that the changes may have been due in some part to an orderly and definite change in the intensity of the epidemic, increasing to a maximum in 1883, and decreasing thenceforward. Whether there was, or was not, any observed variation in the type of disease, apart from the extent of its diffusion, I have no evidence to show. If the analogy with what we have found in certain other towns is real, the cases would, on the average, be more severe in 1883, less so in 1885, and less again in 1887 and 1889. Or, it may be that the apparent maximum in 1883 was due to an excessive number of attacks, the conditions (atmospheric and other) for diffusion being favourable, and that the real maximum of severity (assuming the cyclic hypothesis to hold good here) was to be found in 1885, as at Sunderland.

The South Shields curve, which Munro also gives, is very different. There was greater mortality early in the "seventies", when the record begins, which suggests high mortality in the late "sixties"; but this I have not verified. There was, however, little or no trace of the long curve extending from 1874 to 1890, which is conspicuous in the Jarrow chart.

* Read before the Epidemiological Society, May 20th, 1891.

I have no explanation to offer as to the causes which bring about these major epidemics, if I may call them so; nor am I prepared to say that they must of necessity have the long pedigree and duration which I have tried to trace for them in certain instances. On the contrary, the Norway cycle seems to be complete in five or six years only, and it is quite conceivable that, under favourable conditions, the change might be far more rapid still. We found some indication of a very temporary intensification at Edinburgh in 1883, and it is not uncommon to hear of single local epidemics being attended with heavy mortality. On inquiry, this usually proves to be due to the prevalence of pneumonia, supervening upon mild cases as well as severe. Undoubtedly pneumonia played an important part in the Sunderland and other major epidemics, but that fact will not serve as the explanation of the steady increase of fatality in successive outbursts for ten years, followed by gradual decrease after 1885, unless we credit the pneumonia itself with a tendency to cyclic intensification. This would, of course, open up a wide question whether the pneumonia which accompanies or follows measles is a part of the measles, or a superadded infection, or a mere local complication. Perhaps an increased tendency to fatal pneumonia ought to be counted among the consequences and indications of a severe type of measles.

I trust that I have succeeded in making clear the distinction which I wish to draw between major and minor epidemics of measles. By minor epidemics I mean the familiar outbreaks, large or small, occurring every year or two, and, in a sense, mechanically. But, occasionally, over wide or narrow areas, successive minor epidemics become more and more virulent and destructive, owing, as I suggest, to progressive intensification of the measles virus; and these long waves, built up of many successive minor epidemics, may fittingly be termed major epidemics.

I cannot help thinking that the keynote to the epidemiology of measles is stability of type, amid violent fluctuations in quantity, just as instability is characteristic of diphtheria. In this stability we may find not only some sort of explanation of its usually slow variations in clinical characters, but also, perhaps, a hint as to the real meaning of its little tendency to live outside the human body, of its refusal to be transmitted to lower animals, of the complete absence of any evidence to show that it can thrive in milk

or water, and, lastly, of the failure of all attempts hitherto to grow it in artificial media of any kind.

NOTE.—Dr. Willoughby has very kindly sent me the following translation of a note by Professor C. Ruata, of Perugia : "I have met with a very instructive case, in which measles suddenly broke out in a family, attacking an infant six months old. There was no measles in the village, or in the surrounding country for several miles. The family had no communication whatever with strangers, nor had anyone from elsewhere visited them for a long time. I knew, however, that two years previously a brother of the infant then ill had died of measles, and, consequently, I came to the conclusion that the germs of the disease must have been present in the house itself. On making enquiries, I ascertained that, eight days preceding its attack, the little patient had worn a woollen jacket that his deceased brother had had on during the last days of his life. This jacket had been stowed away in the house without having been previously disinfected, as had been done with everything else. The family was immediately isolated, and there was, in the whole parish, but this single case of measles, although two years before there had been 327, with 22 deaths." (*The Responsibility of the State in regard to the Public Health.* An Address by Prof. Charles Ruata, M.D., of Perugia, 1886. Pp. 10-11.)

EPIDEMIC DROPSY.

By KENNETH McLEOD, M.D., LL.D.

(*Read: January 18th*, 1893.)

I.—Introductory.

It has been my fortune, during my service in India, to witness three invasions of the town of Calcutta by epidemics of rare or new diseases; namely, by Dengue in the year 1872, by Dropsy in the years 1877, 1878, 1879, and 1880, and by Influenza in the years 1890 and 1891. It is to the second of these invasions that I propose to direct your attention this evening, confining reference to the other two to certain epidemiological phases in which they stand in very marked contrast to the subject of this paper. One of these contrasts I may mention at once, namely, that whereas abundant and convincing evidence exists that dengue had previously visited Calcutta—in the years 1824 and 1853 without doubt—and outbreaks of influenza among men and horses are by no means unknown in the sanitary history of the town, no one was able, during the time that this epidemic of dropsy lasted, to adduce any evidence, traditional or written, that anything similar had ever occurred in Bengal. The epidemic therefore presents the always interesting feature of prevalence on a virgin soil. A similar and, as I think I shall be able to prove, identical disease manifested itself at the Hill Station of Shillong in Assam, and in the island of Mauritius in the Indian Ocean, at the time that it was prevailing in Calcutta. An additional interest is therefore imparted to the disease by the opportunity of studying its phenomena in a large town situated within the area of the Gangetic Delta, in a military and civil station placed at an elevation of 5,000 feet above sea-level, some 300 miles distant from Calcutta, and 180 from the nearest sea-board, and in an island of the Indian Ocean near the southern limit of the tropical zone. The epidemic was made the subject of careful observation in each of these places. The evidence collected at the time

is scattered throughout the volumes of the *Indian Medical Gazette* for the years 1878, 1879, 1880, 1881, and 1882. I have drawn up a careful list of the articles containing this evidence, which has been more or less fully utilised and commented upon by Fayrer (28),* Davidson (30), Chevers (27), Moore (29), and others. It happened that, during the years in which the disease prevailed in Calcutta, I held the offices of health officer of the town, editor of the *Indian Medical Gazette,* and secretary of the Calcutta Medical Society. In each of these capacities I strove to elicit information. I visited the affected localities and houses, and saw a great number of the sufferers from the disease. The notes taken at the time are still in my possession, and I shall make use of them in this communication as occasion requires. The reasons that have induced me to trouble the Society with a matter of so many years past, and which possesses no present interest beyond its intrinsic merits, are these:—

1st. No systematic and complete record has as yet been presented of all the facts concerning an epidemic, very rare, if not unique, in its nature, and singularly defined as regards place and time of prevalence.

2nd. The more or less imperfect records which have been compiled have led their authors to different conclusions regarding the nature, causation, and identification of the disease; and

3rd. The facts of the outbreaks which occurred in the three localities which I have mentioned justify the deduction of certain conclusions of an epidemiological kind, which are of a general and present importance, and are well worthy of the consideration of this Society.

II.—Topographical and Meteorological.

Before proceeding to discuss the phenomena of the epidemic, it is desirable that I should describe a few of the more salient features of the topography and climate of the places in which it appeared.

1. *Calcutta.*—The city of Calcutta lies about one degree south of the northern boundary of the tropical zone, and is situated on the left or eastern bank of the river Hooghly, one of the main effluents of the Ganges. It is some 80 miles distant from the Bay of Bengal, and is placed towards the western boundary of the Gangetic Delta. The soil is alluvial, consisting of an alternation of beds of sand and

* The figures in brackets refer to the list at the end of this paper.

clay, covered with a layer of humus of varying thickness and very questionable purity. The subsoil water-level averages 12.4 feet from surface for the year, the variation being from 8.2 in September to 14.7 in May. The average temperature is 79.3°, the average rainfall 65.8 inches, and the average humidity 76 (sat.=100). The seasons may be roughly divided into cold (Nov., Dec., Jan., and Feb.), hot (March, April, May, and June), and rainy (July, Aug., Sept., Oct.). The town area presents the shape of a semi-circle. The Hooghly river is the chord, and the ditch dug in the year 1772, to impede the incursions of the Maharatta horsemen, the arc. The bank of the river is the highest part of the area, and the drainage is eastward, towards the swamps called the Salt Water Lakes. The town area is well drained, but at the time of which I write was copiously pitted with tanks and wells containing very impure water. The town of Howrah stands on the opposite bank of the river, and the rest of the city boundary is encircled by a series of suburban townships, which were then almost destitute of drainage, and in much worse plight in respect of sanitation than the town. The European quarter occupies the southern and western part of the town area, the native the northern and eastern. Collections of huts called "bustees" are scattered throughout the area of both town and suburbs, and were at that time in an infamously filthy state.*

2. *Shillong* is a civil and military station, situated on the northern slope of the Khasia Hills, in the province of Assam, about 2° north of the tropical boundary; elevation about 5,000 feet above sea-level. The surface is uneven, representing a number of knolls, separated from each other by swampy hollows. These knolls consist of transition rocks, sparingly covered with soil, and between them are cretaceous beds, and in the hollows deposits of clay. The basis of the range is granitic. The average temperature is 62.1°, and average rainfall 85.29 inches. The seasons are cold (Nov., Dec., Jan., Feb.), warm (March, April, May), and rainy (June, July, Aug., Sept., Oct.). In these five months about 69 inches of rain fall. The mean daily range of temperature varies from 10.1° in July to 19.3° in January. The climate is considered a healthy one; but the lower parts of the station are not above the level of malarious disease.†

* A very interesting report on the medical topography of Calcutta, by Dr. D. D. Cunningham, will be found in the *Indian Medical Gazette* for 1880 p. 113.

† For a more detailed account of the medical topography of Shillong, see *Climate and Medical Topography of the Himalayan and Sub-Himalayan Districts of British India*, by F. N. Macnamara, M.D., F.R.G.S., p. 191.

3. *Mauritius.*—The island of Mauritius lies about 600 miles east of Madagascar, about 3° north of the southern limit of the tropical zone. It measures 38 miles from N. to S., and 29 from E. to W.; area, 708 square miles, and population about 368,000, of whom 251,000 are Indians, nearly five-eighths of the whole. It presents a central plateau, from 700 to 1,900 feet in height, encircled by ranges of hills, some of which rise to 2,800 feet, and outside of them are plains of varying breadth and altitude, sloping to the sea-coast, which is girt by a coral reef. These plains are intersected by spurs, which enclose valleys and gorges, and are traversed by rivers. Some isolated mountain-peaks crop up in places. Marshes occur on the central plateau, in the neighbourhood of rivers, and on the low land near the coast, and there are tidal inlets which leave mud exposed at low water. The island is volcanic in structure, its rocks and hills consisting mainly of basalt and its varieties. There are traces of metamorphic rocks, but no secondary formations are found. The soils are brown, red, and black. The brown soil is the most common, porous and healthy; the others are more clayey, impermeable and less healthy. The mean temperature is 73.9° on the plains, lower on the plateau and hills; the months May to October being below, and the rest above, the average. There is only a difference of 10° between the lowest and highest monthly means. The mean daily range for the year is 19.1°, the lowest being 16° (March) and the highest 21.8° (November). The average humidity is 73.9 (sat. = 100), the lowest is 71 (November), and highest 77 (May). The rainfall varies at different levels, the higher having the greater fall. A fall of 96 inches occurs on the hills and 68 on the plains. This fall is distributed all over the year, and is liable from year to year to considerable fluctuations. The months of December to May are the rainiest. The climate therefore is an equable one, and the seasons may be divided into warm and wet (December to May), and cool and dry (June to November). Malarious fever was little known in the island of Mauritius till the year 1866, since when periodical and other fevers have been very prevalent. The unhealthy months are from February to July. Both in respect to climate and disease prevalence, therefore, Mauritius presents a remarkable antithesis to Calcutta and Shillong. Drainage and sanitation are in many respects unsatisfactory. The Indian camps are said to consist of thatched houses, often overcrowded, deficient in light and air, generally huddled

together without order, and in close proximity to cow-houses and swine-pens.*

I have summarised the facts which I have now detailed in the form of a table, in which a remarkable contrast is displayed between Calcutta, Shillong, and Mauritius in respect of geology, physical geography, and climate.

COMPARATIVE VIEW OF THE TOPOGRAPHY AND CLIMATE OF CALCUTTA, SHILLONG, AND MAURITIUS.

Particulars.	Calcutta.	Shillong.	Mauritius.
Latitude ...	22° 33′ N.	25° 30′ N.	20° S.
Longitude ...	88° 21′ E.	91° 40′ E.	57° 30′ E.
Elevation ...	18 feet	5000	0 to 2800
Geology	Alluvial; deltaic	Primary and transition; cretaceous beds	Basaltic
Surface ...	Dead level	Uneven; knolls and hollows	Plateau, hills, plains, and littoral
Soil	Clay, sand, humus	Humus; clay in hollows	Brown, red, black
Natural drainage	Slow; imperfect	Good; some stagnation in hollows	Varies
Artificial drainage	Good in town; imperfect in suburbs	Good; capable of improvement	Capable of improvement
Sanitation ...	Indifferent	Fairly good	"
Temperature of the year	79.3	62.1	73.9
Highest monthly mean	86.1° May	69.4° June-July	78.7° January
Lowest "	67.7° Jan.	50.1° December	68.8° July
Difference ..	18.4°	19.3°	9.9°
Mean daily range	14.3°	14.7°	19.1°
Highest	19.7° February	19.3° January	21.8° November
Lowest	8.2° July	10.1° July	16° March
Difference ...	11.5°	9.2°	5.8°
Hot or warm months	March-October	April-October	November-April
Cold or cool months	November-Feb.	November-March	May-October
Annual rainfall ...	65.8 inches	85.29 inches	68.83 inches
Rainy months ...	June-October	May-October	December-May
Dry months ...	November-May	November-April	June-November
Humidity (sat. = 100)	76	77	73.9
Highest	88 August	89 July-October	77 May
Lowest	67 March	57 March	71 November
Difference ...	21	32	6

* *Geographical Pathology*, by Andrew Davidson, M.D., F.R.C.S. This book contains an elaborate account of the topography, climate, and diseases of Mauritius, vol. ii, p. 724.

III.—History of the Outbreak.

The disease first made its appearance in the southern suburbs of Calcutta in the cold weather of 1877-78. It did not attract much attention at that time, and seems to have been confined to a limited area adjoining the river. Its existence was mainly indicated by the fact that it affected Mahomedan tailors, who mostly reside in this locality (Burtolah and Mateabruz), and who take domestic service in European families, returning to their homes after the day's work is over. Many of these were obliged to absent themselves on account of dropsy, which proved fatal in some instances. The disease disappeared during the hot weather and rains, but broke out on the cessation of the latter in its old haunts, and on new ground to the south, south-east, and east of the town. As early as the 4th of September 1878, Dr. Cayley admitted a case into the Mayo Hospital, and on the 11th admitted seven other men, who "all lived and worked together in the same boat, and were attacked with illness on or about the same day" (1). The outbreak of 1878-79 exceeded that of the previous year to a considerable extent, both as to extent of area infected and number of cases. Dr. Rammay Ray, on his return from famine duty in Madras, in January 1879, found the disease prevailing extensively in the southern suburbs, (Bhowanipore, Kidderpore, and Ballygunge). Drs. McConnell and Harvey, who held the office of Civil Surgeon of the district surrounding Calcutta, investigated the matter, which had now excited public attention, and reported officially that the disease was very prevalent in the southern suburbs (Garden Reach, Alipore, and Bowanipore), and was causing a great deal of sickness and mortality. Cases were being sent to the hospitals from the villages, and medical practitioners were now called to attend numbers of persons suffering from a dropsical disease which they had never before met with. With the advent of the hot weather the disease again disappeared, and remained dormant during the rains, at the close of which it again broke out, reappearing in the southern suburbs in October and November 1879, breaking out also in the eastern suburbs (Kurryah, Baniapooker, and Sealdah), and in some parts of the town-area situated at the south-east (Bamun Bustee, Park Street, Collingah and Taltollah), in the immediate neighbourhood of the affected suburban area. Attention was now thoroughly roused to what appeared to be a spreading and increasing

plague. Reports were called for by Government, investigations were conducted by the Health Officer, medical practitioners made careful observations and inquiries, and a good deal of information was in one way or other obtained. The result of a police investigation in January 1880 showed that 214 deaths had taken place both in town and suburbs during the cold weather of 1879-80; and that, while cases occurred sporadically throughout town and suburbs, the disease was mainly incident over the limited areas which I have indicated.* The picture presented to us by this brief sketch is of a novel disease, whose main characteristics were dropsy, fever, bowel complaint, and anæmia, invading a limited area of the suburbs in the cold weather of 1877-78, disappearing during the rains of 1878, breaking out afresh over a more extensive but adjacent and still limited suburban area in the cold weather of 1878-79, again vanishing in the hot weather and rains of 1879, and finally showing itself with increased intensity over a still wider suburban and contiguous but limited urban area in the cold weather of 1879-80, disappearing, not to recur again, as the hot weather of 1880 advanced. We have thus to do with three periods of prevalence and two intervening periods of latency. Of the conditions affecting this interesting epidemic, as regards its nature, subjects, and their environment, I shall have more to say presently.

The outbreak at Shillong commenced in October 1878, at the same time that the second recrudescence was taking place in Calcutta. The disease was first observed among Bengali clerks and their families and households. It was limited to no special part of the station. Cases continued to occur until the warm weather of 1879 set in, when it vanished. It affected Bengali clerks, sepoys, Assamese ,

* The following return of deaths was obtained for the first quarter of 1880 :—

	Mixed Races.		Hindus.		Mahomedans.	
	Males.	Females	Males.	Females.	Males.	Females.
January	—	—	5	9	3	4
February ...	—	1	17	14	18	33
March	—	—	6	5	6	22
	—	1	28	28	27	59
	1		56		86	
			143			

and more sparingly Kasias and Ghoorkhas, but did not spread to the valleys surrounding the station (3, 10). Dr. O'Brien, who was civil surgeon of Shillong at the time, had served eight years in Assam, and had not seen any similar disease.

An outbreak of the same disease took place in January and February 1879, in the town of Dacca, where it attacked all classes of society except Europeans (Crombie, 6). And it prevailed in South Sylhet among coolies on tea-gardens in the cold weather of 1878-79 (Nairne, 9). There is also reason to believe, though definite information is wanting, that the dropsical affection appeared to a large extent in other parts of Assam and Cachar about the same time.

While these events were happening in India, a disease, which I shall presently show was identical, broke out in the island of Mauritius, in November 1878, among Indian coolies in the district of Moka, on the central plateau. A rapid increase of cases took place in that district during the two succeeding months. The outbreak reached a climax in February 1879, and subsided in April. In December the epidemic extended to the district of Plaines Wilhem, also on the central plateau, and Port Louis, on the western coast; in January 1879, to Savanne, Pamplemousses, Flacq, Riviere du Rempart and Black River—all littoral districts; and in February it appeared in the district of Grand Port—also a littoral district to the south-west. It thus invaded almost the whole area of the island. It subsided in June, and practically died out soon after. The disease confined itself mainly to Indian coolies, and it was observed that coolies imported from Calcutta suffered more than those imported from Madras. The general population suffered to some extent in the town of Port Louis; Europeans were entirely exempt from the malady. Seven hundred and twenty-nine deaths were reported to have been caused by the malady, and as the death-rate was estimated to be 2 or 3 per cent. of cases, some twenty or thirty thousand persons must have suffered from the disease—equal to about one-tenth of the coolie population.

IV.—Symptoms.—General Description.

The symptoms of the disease which prevailed in the places and at the times which I have indicated are concisely shown in the following scheme which I have drawn up from the Report of the Health Officer of Calcutta, the Civil Surgeon of Shillong, and the Chief Medical Officer of Mauritius.

	Calcutta.	Shillong.	Mauritius.
(*a*) Dropsy ...	Dropsical swelling of the limbs; the lower always, sometimes the upper; occasionally the body and face.	Œdema of lower extremities; sometimes of upper; occasionally of trunk and face.	Anasarca of lower extremities; often of upper extremities and trunk; occasionally of face. Effusion into cavities rare.
(*b*) Pyrexia ...	Fever sometimes before and sometimes after the swelling, persisting in some cases, and in others altogether absent.	Fever of a mild type preceding, accompanying, or following swelling in most cases; rarely absent.	Mild fever, in some cases preceded by rigors, irregularly intermittent or remittent in type; high fever, sometimes due to complications.
(*c*) Disorder of stomach and bowels	Bowel complaint in many cases; diarrhœa most commonly, dysentery in a few.	Irritability of bowels, sometimes amounting to looseness, which occasionally preceded swelling.	Attack generally ushered in by vomiting and purging, in majority subsiding in a few days.
(*d*) Neuroses	Burning and pain on and in the affected limbs at commencement.	Burning and pricking of skin and pain in limbs in most cases; usually an early symptom.	Deep-seated pains in body and limbs, and sometimes in epigastrium. Occasionally burning and heaviness.
(*e*) Eruption ...	Purple or livid discoloration of the skin in some cases, disappearing on pressure.	No eruption or discoloration of skin noted.	Rubeolar rash in many cases; petechiæ and phlyctenæ in some.
(*f*) Urine ..	Scanty or excessive flow of urine; no albumen.	Increased frequency of urination in some cases; no albumen as a rule.	Urine varied in colour and quantity; seldom contained albumen.
(*g*) Dyspnœa, cough, etc.	Dyspnœa, cough and palpitation in most cases.	Dyspnœa on exertion in some cases; urgent in a few.	Dyspnœa not uncommon; severe and paroxysmal in some.
(*h*) Anæmia, etc.	Great emaciation, prostration, and anæmia in severe cases, slighter in others; well-marked in all.	Anæmia and cachexia in all cases, supervening or increasing during progress of disease; scurvy uncommon.	Anæmia well-marked in most cases; red corpuscles diminished; white increased, with granules.
(*i*) Duration of illness	Duration about two months on the average. Great enfeeblement and ill-health, with persisting anasarca for long in many cases.	Duration of illness one month or six weeks; anasarca and debility, tending to persist.	Duration 3 to 6 weeks; œdema of feet often continued after every other symptom left.
(*j*) Mortality	Mortality considerable; estimated from 8 to 40 per cent. Great dyspnœa in fatal cases; death often sudden and early.	Mortality slight; result in fatal cases due to chest complications.	Mortality about 2 or 3 per cent.; higher among the old, feeble, and cachectic.

This comparative scheme, which gives a fairly complete view of the principal features of the disorder, makes it quite certain that the disease which prevailed in the three places was essentially the same. The skin eruptions and early gastric and intestinal disturbance were more frequently met with in Mauritius, and the type of the disease seems to have been milder both in Shillong and Mauritius than in Calcutta, but these differences are capable of explanation. The detail of symptoms given by Dr. Crombie from Dacca (6) and Dr. Nairne from South Sylhet (9) accords very closely with the particulars noted in this table.

V.—Analysis of Symptoms.

Taking, as there seems every reason to do, the descriptions of the disease furnished by observers in India and Mauritius to refer to the same thing, I now proceed to the study of the facts noted as regards each of the classes of phenomena presented in the foregoing table.

1. *Dropsy.*—This constitutes the most prominent, and apparently the essential and indispensable feature of the disease. Other symptoms might or might not be present; this was constant, unless we except a few cases of fever and diarrhœa (O'Brien, 3), or fever and exanthematous rash (Chambers, 16), occurring in the same household as the dropsical disease. These, however, were very rare. The dropsy was preceded in some cases by fever; in others, by vomiting and diarrhœa; in others, by burning, tingling, or pricking of the skin: these may, under such circumstances, be accounted prodromata, and they preceded the swelling by one to three or four days. In many cases these symptoms occurred simultaneously with the appearance of the swelling; in others they occurred consecutively; and in not a few the swelling, associated perhaps with some anæmia, and general debility, was the only symptom present. Among 33 of the 35 cases which I have collected from various sources (appended), in 21 the swelling was preceded by other symptoms; in 6 it was the first symptom noticed; and in 5 the other symptoms appeared simultaneously with it. The swelling usually made its appearance in the lower extremities—feet and legs—and proceeded upwards. In some cases the lower extremities were the only part of the body affected. In others it ascended to the hips, and reached the waist. The scrotum was often swollen in males. The upper

extremities were often affected, and the face and neck more rarely. Among the 35 cases which I have tabulated, the lower extremities were affected in all; the upper extremities in 12; the trunk in 9; and the face in 7. In 2 cases the anasarca was general. The tensity of the swelling varied, according to the stage of the malady. In recent and severe cases it is described as firm and tough, or hard and brawny. In older cases it was less dense and stiff, and pitted more easily. The skin of the swollen parts was, in some instances, congested and erythematous, and, at later stages, furfuraceous or desquamating. Vesicles, phlyctenæ, and ulcers are described, but were rare. The swelling was also very persistent, lasting and recurring after the patient was otherwise well. It tended to subside or disappear at night, and recurred during the day. This was evidently due to position. Accumulations took place, in some instances, in the pleuræ and pericardium, very seldom, if ever, in the peritoneum; but these were rare. Œdema of the lungs was not uncommon in severe cases, evidenced by rough and moist auscultatory sounds and diminished resonance on percussion. Anatomically, the accumulation of serous fluid was found, on *post mortem* examination, to take place mostly in the skin and subcutaneous areolar tissue. In two cases examined by Dr. Tamiz Khan (16), the serum oozing from the divided cutaneous and subcutaneous textures was found to be sanious, while the fluid effused elsewhere was clear. Serum was also found in the deeper tissues, intermuscular areolar tissue, etc., in the pleuræ, pericardium, and ventricles of the brain, and the lungs were œdematous or carnified. Intercranial and intraspinal effusions seem to have been rare and scanty (Lovell, 26). There were no signs of inflammation found either during life or after death.

2. *Pyrexia.*—Fever was a very constant feature of this malady in all three places. It was very often the first thing that occurred, and anticipated the appearance of dropsy by one to four days. In the 35 cases which I have tabulated, pyrexia was noted in all but 3, and was initial, that is, preceded the swelling, in 14. In one case the temperature was found to be subnormal (R. D. Ghose, 14). In other cases the fever either accompanied the development of the swelling, or appeared after that had set in. The pyrexia was rarely ushered in by a well-marked rigor. Crombie distinctly notes that the fever which accompanied the anasarca at Dacca was "without rigors" (6).

All the Indian observers omit this symptom. On the

other hand, Dr. Lovell states that many of the Mauritius patients experienced rigors; but he is inclined to attribute this to an aguish habit, which is apt to be fanned into activity by any bodily disorder (26). The type of the fever seemed to be a mild remittent. It occurred mostly at night, and many temperatures of 99° and 100° were noted; in some instances Dr. Lovell writes of morning temperatures of 99° to 100°, and evening temperatures of 100° and 101° (26). Dr. Harvey, on one occasion, took the temperatures of six members of a sick family, and found them to be 99°, 100°, 100.9°, 101°, 101°, and 102.8°. Higher temperatures were noted—as high as 104°—but these were either in malarious subjects, or in those suffering from pneumonia or other serious complication. The terms applied to the pyrexia were: "fever", "night-fever with pains", "temperature slightly raised", "distinct fever", "irregular fever", "quotidian and irregular quotidian", "remittent and mild remittent". No mention is made of sweating by any observer.

On the whole, it is evident that (1) pyrexia was a frequent, if not constant, symptom of the disorder; (2) that the fever preceded, accompanied, or followed the swelling; (3) that rigors and sweating were rare; (4) that the elevation and range of the temperature were moderate; and (5) that the fever did not present the features of what is ordinarily known as malarious fever, except in subjects who had previously suffered from that type, and had chronic enlargement of spleen.

3. *Disorder of the Stomach and Bowels.*—In the Mauritius epidemic, it is stated that "the disease was, in most instances, ushered in by diarrhœa and vomiting" (Lovell, 26). The diarrhœa subsided in a few days, and the vomiting was "accompanied with slight nausea and considerable epigastric distress, often amounting to pain". In a few cases these symptoms appeared after the dropsy was established. In Calcutta and Shillong the gastro-intestinal irritation was not so common or definite a symptom; but it was frequently present both in the earlier and later stages of the complaint. Bowel-complaint is mentioned in 14 of the 35 tabulated cases, and in 6 it was initial. Calcutta observers make frequent mention of diarrhœa and dysentery occurring in course of the malady. Dr. Cayley found that three or four out of the seven boat cases recorded by him had vomiting and diarrhœa at the beginning of the attack (1). Many of the village cases seen by myself gave a history of diarrhœa and dysentery. Dr.

Kastagir lays special stress on the irritable state of the bowels, diarrhœa and dysentery occurring spontaneously, or being set up by a mild purgative (12). Dr. Tamiz Khan draws attention to the frequency of piles and painful defæcation in his cases (16). The bowel-complaint was often associated with fever, and it did not appear to cause any diminution of the swelling. Dr. O'Brien found that frequent calls to stool, with scanty motions, constituted a trouble in many of his cases (3). Constipation, or constipation alternating with looseness, is noted in some of the cases recorded.

4. *Disorder of the Nervous System.*—Skin irritation and deep-seated pains in the limbs are a decided feature of the disease. The skin irritation is described as a burning, or pricking, or itching, or feeling of painful distension. It often preceded the appearance of the swelling, and was in some instances limited to the soles and hands. The more deeply situated aching was referred to the muscles, bones, and joints, and constituted in most cases a distressing condition. The lower extremities were most commonly the seat of these aches, but the loins, and sometimes the whole body suffered. These pains were often associated with fever, and seemed to be worse at night. These symptoms subsided as the swelling abated. No mention is made by any of the observers of numbness, either partial or general. Stiffness and heaviness are alluded to, but attributed to the effusion. Paralysis was absent. Dr. Lovell does not mention it among the symptoms, and states explicitly that "paralysis was never seen in acute anæmic dropsy" (26). Dr. Rammay Ray positively records that in 650 cases which he had seen (500 in the Madras Presidency and 150 in Calcutta) he had not seen paralysis in one single case. The only observer who found anything like paralysis was Dr. Harvey, who in two cases noted that there was an approach to paralysis of the lower limbs, as if from effusion of serum into the spinal canal, and in a good many more there was difficulty in walking, apparently not due to paralysis, but to the local condition of the limbs (14). This absence of paralysis is an indisputable fact, and will be again referred to when I come to discuss the identification of the disease.

5. *The Eruption.*—An eruption on the skin was more frequently observed in Mauritius than in any of the other places in which the disease was studied. Dr. Lovell states that it was seen in a large proportion of cases; but refers to the difficulty of detecting a rash on the "swarthy skin of the Indian". This difficulty, together with the fact that

the Indian cases were commonly seen in their later stages, accounts, in my opinion, for the comparative infrequency with which the rash was noted by Indian observers. Dr. Lovell states that "on the face it was generally observed as a diffused redness; on the trunk, thighs, and arms it presented a morbillous appearance—dark red, somewhat crescentic patches, about two to four lines in diameter, enclosing patches of healthy skin; on the legs, below the knee, it was generally, though not always, diffused, presenting the characters of erythema. The redness disappeared on pressure. In bad cases petechiæ were seen along with the eruption. Phlyctenæ bullæ and desquamation were the usual sequelæ of the eruption" (26). It is said to have appeared about a week after the œdema, and continued for about ten or twelve days. It disappeared after death. In Calcutta this symptom was not so commonly observed. Dr. Cayley in one of his cases saw a decided red blush over the face and chest (1). Dr. Juggobundoo Bose observed a redness of the skin like scarlatina, which preceded the swelling (14). Dr. Harvey noted a mottled skin (14), and Dr. Nicholson purpuric spots (14). Dr. Debendra Nath Ray observed a rash on the lower extremities and abdomen in one case (16); and Dr. Rammay Ray described desquamation in a certain number of cases during convalescence (15). Dr. Tamiz Khan observed blueness and lividity of the swollen limbs and intolerable itching of the whole body, succeeded by rash, preceding the swelling (16). In the village cases which I examined (most of them of long standing) I noticed claret-coloured discoloration of the skin of the lower extremities in one case, dull colour of the skin in another, desquamation in a third, purple discoloration with purple pimply spots in a fourth, and ulcers of the legs discharging sanious fluid in a fifth. Dr. Crombie does not record a rash in the Dacca cases, nor Dr. Nairne in the Sylhet cases, nor Dr. O'Brien in the Shillong cases. Dr. Chambers, who saw the disease mostly among Calcutta Eurasians, and in the earlier stages, describes "a scarlet efflorescence from the beginning of the disease especially confined to the face, neck, upper part of the thorax, and the extremities, or petechial spots with circumscribed measly eruptions on face and trunk, or large purpural or mulberry patches. In infants a marbly, mottled, purplish, or red tinge of the skin, especially of the extremities, neck, and cheeks" (16). This description tallies very closely with the quotation which I have given from Dr. Lovell's paper. Dr. Chambers records a group of cases which I shall quote:

"In 1878 I attended a Eurasian family in Dhurrumtollah Street, on the ground floor of an upper-roomed house. All the inmates, numbering seven, together with two visitors, were affected with fever, scarlet efflorescence, and eczema of the legs; while two of the male native servants soon took the infection, got swelled legs, and discontinued attendance." These statements render it certain that an exanthematous eruption was a feature of the disease in a certain proportion of the Calcutta cases.

6. *The Urine* was carefully examined by competent physicians in Calcutta, Shillong, and Mauritius, and these all concur in stating that, as a rule, it did not contain albumen. In other respects the secretion varied, as Dr. Lovell puts it, in colour and quantity. Some observers mention excess, others deficiency. Micturition was increased in frequency sometimes, and evidence of irritation of the urinary organs existed. In other cases the secretion seems to have been scanty, and its discharge infrequent. The specific gravities noted by Dr. O'Brien are normal for natives. On the whole it appears that no alterations took place in the fluid which might not be attributed to the pyrexia which existed in most cases. Unfortunately, no microscopic examination seems to have been made of the fluid.

7. *Dyspnœa and Disorder of the Heart and Lungs.*—Disturbances of respiration and circulation were quite a prominent phenomenon in this disease. In slighter cases there might be simple breathlessness on exertion; in the more severe distressing orthopnœa was common. Filling of the cavities and œdema of the lungs appeared to be the causes of these disorders. A slight cough with mucous expectoration was a frequent symptom; while in a few cases a hacking cough with prune juice expectoration betokened congestion or inflammation of the lungs. These conditions gave the usual physical indications on auscultation and percussion. Dr. Kastagir met with some cases of catarrh and coryza (12). Dr. Rammay Ray, who from an experience of 650 cases writes a very intelligent and elaborate description of the disease (15), gives an excellent account of the morbid conditions of lungs and heart apt to be met with in severe cases. He describes increased rapidity (ninety-six per minute), and oppression of breathing, anxious look, livid lips, and cold extremities, dry hacking cough, frothy mucous expectoration, dulness of bases, bronchial breathing, increased vocal resonance, sibili, rhonchi and crepitations and signs of pleuritic effusion.

As regards the heart he notes acceleration, intermittency and weakness of pulse (50 to 180 per minute), violent palpitation, increased precordial dulness and murmurs, which he attributes to anæmia, dilatation and thickening of the valves. These things were found in bad cases, and the testimony borne by this observer was confirmed by myself and others. He observes that these disorders of the heart and lungs tend in their turn to increase the dropsy, and this is extremely likely.

8. *Anæmia, Scurvy, and other Constitutional Derangements.*—"Anæmia", writes Dr. Lovell, "was an essential feature of the disease." The truth of this observation is supported by all who saw the disease. Dr. Rammay Ray found anæmia present in nearly 94 per cent. of his cases; but states that in 40 cases out of 650 there was no anæmia present. Dr. O'Brien found many of his cases anæmic; but observed that some, who were not anæmic before being attacked, became so as the disease progressed; and that in others the anæmia got worse as the disease advanced. It is quite certain that some of his cases were quite free from anæmia before the attack; others are described as cachectic (3). Dr. Harvey found anæmia to be a constant condition; is not sure whether it was a cause or a consequence, and remarks that "it may very likely be a consequence" (14). Dr. D. B. Smith describes hæmic murmurs (11 and 14). These were observed by Harvey and others. Dr. Lovell examined the blood, and found the red corpuscles diminished in number, and the leucocytes increased together with granules and molecules. Observations made by Drs. Juggobundoo Bose and Tamiz Khan are to the same effect. The late Dr. T. R. Lewis examined the blood and found nothing special in it. Evidences of a scorbutic dyscrasia were less marked than of anæmia. The season was one of high prices and insufficient nourishment, and a large proportion of the lower classes of natives of India suffer from swollen and sore gums, simulating, if not indicating scurvy. Dr. Rammay Ray noticed scorbutic gums, with occasional bleeding from them, and other symptoms of scurvy present in "several" cases. Dr. Harvey, Dr. O'Brien, and myself observed similar appearances in many cases; but it is absolutely certain that the disease affected persons in excellent health, without a suspicion of scurvy, and that the majority of those seized with it developed no sign of scurvy throughout its course. Dr. Lovell states that "patients, as a rule, exhibited no signs of cachexia up to the period when the diarrhœa and

vomiting commenced" (26). He makes no mention of scurvy. Dr. O'Brien considers the existence of signs of scurvy in some of his cases accidental.

The disease was no doubt a very debilitating one, and caused great wasting, pallor, weakness, and prostration in persons severely affected; but these constitutional conditions were in many undoubtedly, and in most or all probably, produced or aggravated by the disease, and were consequences, not causes.

9. *State of Spleen and Liver.*—As might be expected among the class of persons principally affected, and at the season when the disease prevailed, more or less enlargement of the spleen was observed in many of the sufferers; but all the observers, Dr. Lovell included, considered this an accidental circumstance, and in no case was it observed that the organ underwent enlargement during the progress of the malady. Dr. Rammay Ray, who had the largest experience of the disease, explicitly states that "the spleen was seldom found enlarged" (15). On the other hand, the same observer found that "the liver, healthy in the beginning, occasionally became enlarged and painful on pressure, and that only when the lungs and heart were gravely involved". This experience was confirmed by other observers. Dr. Lovell states that "the lymphatic glands were not enlarged, painful, or otherwise visibly affected".

10. *Duration of the Disease.*—The disease ran in most cases a protracted course. Two or three months was the general estimate in Calcutta. Dr. Nairne, in South Sylhet, found that in mild cases recovery took place in from four to ten days, and in severe cases in three or four weeks. Dr. O'Brien's cases lingered on for weeks, and Dr. Lovell pronounces three to six weeks to be the ordinary length of an attack. Some cases pursued a more severe and rapid career. Dr. Rammay Ray observed the disease to prove fatal within five days of its commencement. He cites a case that died on the sixth day. He had heard of the disease proving fatal within twenty-four hours, and he alludes to sudden death being not unfrequent (15). Dr. Chambers (16) and others give similar testimony.

11. *Sequelæ.*—Beyond general weakness, some anæmia, and persisting œdema of legs, the disease does not appear to have caused any serious or permanent derangement of health or organic integrity. Some cases were so mild that the patients continued to pursue their ordinary avocations. Even severe cases recovered their usual health satisfactorily. Take, for example, Dr. Nicholson's experience in the General

Hospital, where he treated six cases, all profoundly anæmic, one showing purpuric spots. They had much dyspnœa and palpitation. Yet he reports that "two of the cases recovered perfectly, and the others were doing well". Dr. Lovell also states that the disease left the patient in perfect health after a comparatively short course.

12. *Mortality.*—This varied considerably, and appears to have been heavier in Calcutta than elsewhere. Dr. Rammay Ray found the death-rate among his cases to be 8 per cent. (15). The returns collected for me through the agency of the police gave a death-rate of about 20 per cent. for the town and 44 for the suburbs; but it is probable that the milder cases escaped notice. Some statistics which I collected personally in the villages gave a rate of 18.6. Dr. Harvey discovered a rate of 25 per cent. in one locality; two, three, or four deaths in a family were noted by several medical men. On the other hand, Dr. Nairne states that there were no deaths among the affected coolies in South Sylhet (9). Dr. O'Brien records fatal cases at Shillong, but they were evidently few (3). Dr. Lovell estimates the Mauritius mortality at 2 to 3 per cent.

VI.—Morbid Anatomy.

The information under this head is somewhat scanty. Dr. Lovell supplies some notes derived from a few autopsies (26). Dr. Tamiz Khan contributes a detailed report of the careful examination made by himself and Dr. McConnell (16). The main facts are these:

1. *Skin and cellular tissue* throughout œdematous; skin livid; texture of skin and subcutaneous areolar tissue hard and brawny, almost gristly, emitting on section sanious fluid; fluid effused into deeper tissues, and cavities quite clear; subcutaneous extravasations found. Dr. Tamiz Khan observed in one of his cases punctate extravasations of scalp, pericardium, and peritoneum, and a patch of extravasation in the ventricular septum; no sign of inflammation.

2. *Head.*—Brain healthy, as a rule; a little fluid in ventricles in some cases; substance of brain said to be œdematous in a few cases. In the Calcutta cases the brain-substance was found to be firm.

3. *Chest.*—*Pleuræ* contained more or less clear fluid; lungs œdematous. *Pericardium* also contained some fluid. *Heart* soft, flabby; cavities contained soft dark clots or fluid blood; muscle fatty, no valvular disease, no decolorised clots in pulmonary artery or aorta.

4. *Abdomen.*—No ascites; *stomach and intestines* congested in the Calcutta cases; *liver* large, soft, fatty, with well-marked interlobular congestion; *spleen* normal in Calcutta cases; normal, enlarged, and atrophied in Mauritius; *kidneys* congested, cloudy swelling of epithelium; no other disease; *mesenteric glands* enlarged and injected in Calcutta cases.

5. *Spinal Canal.*—This was only examined in one instance in Mauritius. The membranes were found congested, and lumbar enlargement softened.

6. *Vessels and Blood.*—The large veins were carefully examined by Tamiz Khan, and found healthy. The blood was dark and fluid; no sign of thrombosis or phlebitis was seen; the blood presented an excess of leucocytes and granular material.

In the Calcutta cases death seems to have been due to apnœa, and the lividity and congestion described seem to be owing to that circumstance.

These observations indicate that the œdema constituted the principal pathological as well as symptomatic feature of the disease, and it is important to note that the effusion into the tissues was more marked than into the cavities. Also, that this effusion took place throughout the body, and did not appear to be materially influenced by gravitation.

Having described the phenomena of the disease as fully and accurately as the materials at my disposal permit, I proceed now to consider its epidemiology, and this may be conveniently done as regards (1) subject; (2) environment; and (3) origin and diffusion. Having stated the available facts under these heads, the questions of causation and of identification can be appropriately discussed.

THE ENVIRONMENT.

It will be more convenient to take up the subject of environment, or the influences—local, climatic, and hygienic—to which the individuals who contracted the disease were subjected at the time in the first instance. These may be displayed under the heads of (1) Place; (2) Season; (3) Food and Water; (4) Hygienic conditions; and (5) General salubrity of the period of prevalence.

VII.—Local Conditions.

The disease prevailed, as we have seen, in localities very differently circumstanced as regards geology, soil and surface, elevation and distance from the sea. It certainly

appeared first and lingered longer in alluvial deltaic Calcutta than in hilly Shillong or insular Mauritius; and the parts of Calcutta in which it was most common and persistent were the more swampy and worse drained suburban areas; but the local conditions under which the disease originated and spread were so various that topical influences cannot be alleged to have had much control over its appearance or diffusion. In the island of Mauritius the disease prevailed in the more elevated and central, as well as the flatter, lower, and littoral districts indifferently.

VIII.—Meteorological Conditions.

The years 1876 and 1877 are memorable in India on account of the failure of rain which took place in Southern India, and the consequent severe and wide-spread famine. Bengal and Assam were not included in the famine area, but they were indirectly affected by the scarcity of food elsewhere. The climate of Calcutta in 1877-78 and 1879 was in no way exceptional, but this disease nevertheless exhibits a very remarkable dependence on meteorological conditions in that it broke out on three several and successive occasions at the close of the rainy season, remained active during the cold season, and became dormant twice, and finally vanished as the weather became hot. The rainfall of 1877 was 60.96 inches, of 1878, 55.55, and of 1879, 43.51; average, 65.8. The rainfall of these three years was therefore moderate. At Shillong and elsewhere in Bengal the period of outbreak and prevalence was the same, but there was no latency nor repetition. Dr. McConnell thought that an unusually severe and late flooding had something to do with the outbreak of 1878-79 (7); and Dr. O'Brien surmised that a heavy and protracted rainfall may have determined the Shillong outbreak (3); but after events, and the incidents of prevalence elsewhere, deprive these speculations of weight. The rainfall of Shillong in 1878 amounted to 107.53 inches, considerably over the average. Dr. Lovell's testimony is worthy of quotation *in extenso*. "Climate and season", he states, "seemed to have no influence on the spread or mortality. It began in a district which is reputed to be healthy and free from malaria, and it afterwards spread to the unhealthy districts, but it did not appear to be either more common or more fatal in the latter place than in the former. It first appeared in the healthy season after a long drought, but the change of season and the supervention of the rains did not stay its

progress or modify its character. In fact, it commenced under one set of climatic conditions and spread and continued through another" (26). Epidemic diseases in India are greatly influenced by seasonal conditions. This was remarkably illustrated by the great dengue epidemic of 1872, which prevailed and spread as long as the hot weather lasted, and died out when the cold season set in, failing subsequently to overstep the limits where in its first year of prevalence it had encountered the depressed temperature. The outbreak of influenza in India also took place in the hot weather, but its spread was so rapid and complete that it is difficult to say whether its cessation was due to exhaustion of pabulum or to meteorological influence. It is interesting to note, however, that, after dormancy during the rains and cold weather of 1890-91, there was a recrudescence of the disease in Calcutta in the hot weather of the latter year.

IX.—Dietetic Influences.

There can be no question that, in consequence of the Madras famine, the price of food in Calcutta and throughout Bengal and Assam was unprecedentedly high in the years 1877-78 and 79. Rice sold at double its usual rate, and the lower classes undoubtedly were under-fed.* There was also an influx into Calcutta of half-starved folk from the famine districts. This circumstance may perhaps explain the amount of scurvy and general ill-health observed in many of the Calcutta cases, and probably accounts for the higher mortality which took place in that town. But even in Calcutta it is beyond doubt that the disease was by no means confined to the ill-fed. I found that well-fed, robust, and healthy persons were attacked by the disease equally with the debilitated, cachectic, anæmic, and scorbutic. The testimony of Drs. Cayley, O'Brien, and Harvey is to the same effect, and Dr. Rammay Ray observed that hundreds of persons exhibiting these dyscrasiæ remained free of the disease. He pronounces these, as well as other alleged factors, such as damp, wet, and cold, to be "rather the nurse than the parent of the disease" (15). Dr. Lovell, while conceding that the diet of Indians in Mauritius is of

* Price of a maund of common rice :—

	Rs.	As.	Pce.		Rs.	As.	Pce.
1875 ...	2	8	0	1878 ...	3	3	6
1876 ...	2	12	0	1879 ...	2	12	0
1877 ...	3	12	0	1880 ...	2	0	0

low nutritive value and predisposes to anæmia, does not assign to it a determining influence in the causation of this dropsy. There is no evidence to indicate that water or any other ingesta exercised any causative or aggravating effect.

X.—Hygienic Conditions.

The classes mainly affected in Calcutta lived under influences exceedingly unfavourable to health, but both in Calcutta and Shillong persons better circumstanced in these respects suffered, and in Mauritius there is no evidence that domestic or personal hygiene was in any respect or degree more unfavourable to health during the prevalence of this malady. The only Indian observer who attached importance to this kind of influence was Dr. Kastagir, who found that the disease broke out in damp, dirty, ill-ventilated houses in preference to others (12). Defective hygiene must, therefore, along with some of the other influences already noted, be relegated to the class of adjuvants.

XI.—General Insalubrity.

The period during which this disease prevailed in Calcutta was undoubtedly what may be called a "bad time". The general death-rate was very high. The rate for 1877 was 31.9 per 1,000; for 1878, 38.1; for 1879, 30.3; and for 1880, 27.1: the mean rate for the decennium 1871-80 being 28.7; and of the decennium 1880-89, 27.5. The suburban rates were considerably higher. The deaths for fever in the years 1876, '77, '78, '79, and '80 were 4,361, 5,131, 6,086, 4,796, 3,797, and 3,765. Most of the deaths from epidemic dropsy were, according to the health officer, registered under this head. The deaths caused by cholera during these years numbered 1,851, 1,418, 1,338, 1,186, 805, and 1,693: all high figures with exception of 1879. There was an epidemic of small-pox in 1878-79, the mortality amounting to 1,495 and 772, against 71 and 67 for the two preceding, and 114 and 133 for the succeeding years. There was a slight increase in the number of deaths registered under dropsy during 1878-79, and '80, but so slight as to indicate that deaths caused by this epidemic were returned under other heads. Rinderpest also prevailed severely among milch and draught cattle in the town in November and December 1879. Altogether the "epidemic constitution" of Calcutta during these years was

bad. Similar evidence is absent as regards Shillong and Mauritius.

THE SUBJECT.

The particulars affecting the personal conditions of the victims of this disease may be considered under the heads of: 1. Race (including nationality and caste); 2. Social conditions (including occupation and rank in life, and social habits); 3. Sex; 4. Age; 5. State of health at the time of attack.

XII.—Race.

It is a very remarkable feature of this disease that it prevailed, in all the localities which it visited, mostly among persons of a particular race or nationality. In Calcutta natives were by far the greatest sufferers, although it also attacked a few Eurasians and Armenians. And among natives, Mahomedans seemed to get it more frequently and severely than Hindus. The earliest victims were Mahomedan tailors and boatmen, and subsequently it seemed to declare a preference for Mahomedan communities and households (Rammay Ray, 15). As the malady became more general this preference was not so marked. Europeans were entirely exempt. At Dacca "the disease attacked all classes of society except Europeans" (Crombie, 6). At Shillong it appeared and spread among Bengalis and Assamese associated with them. A few hill people, Khasias and Ghoorkas, were affected, but this was exceptional, and no European was attacked (O'Brien, 3, 10). In South Sylhet the disease was confined entirely to the coolies labouring on tea-gardens (Nairne, 9). In Mauritius, also, it was Indian coolies who were first and most affected; and amongst these, coolies imported from Calcutta were attacked in larger proportion than Madras coolies. The disease spread to some extent among the general population of the town of St. Louis. Here, also, Europeans were entirely exempt. These facts are very definite, and present a strong contrast to the behaviour of the epidemics of dengue and influenza, which appeared to be indifferent to race, or sex, or age.

XIII.—Social Condition and Habits.

Oriental races are apt to be gregarious and exclusive; their habits of life are simple and similar. The persons and communities affected differed greatly from each other

as regards occupation, social status, wealth, and, to some extent, habits. But it seemed as if whatever social stratum or class first became affected, the disease tended to attach itself to persons belonging to that class or community. Poverty, destitution, privation, exposure, fatigue, and the like, did not seem to determine the incidence of the disease to any appreciable extent. "Rich and well-to-do people", Dr. Harvey remarks, "well-fed, and living in elevated and very dry houses, have been attacked quite as freely as poor and ill-fed people living in damp huts on the ground level" (14). The experience of other Calcutta observers was to the same effect. The coolies on tea-gardens are well fed and housed and clad, and there was no starvation or distress among the Indian coolies at Mauritius. The disease commenced in Calcutta among a well-paid class of artisans, the Mahomedan tailors; and at Shillong it appeared first, and continued to affect in largest proportion government clerks, and their families and domestic servants, who did not want for food or other necessaries of comfortable life. It would appear from these facts that the racial proclivities of this disease depended rather on the gregariousness and exclusiveness of the communities affected than on anything special in their social habits, occupations, or other personal peculiarities of individuals. The disease was singularly discriminative, but grouping and association seem to have constituted the principle and basis of selection. This is evidently the opinion of Dr. Lovell, whose remarks on the subject are worthy of quotation. "The Indian, whether engaged as a labourer or otherwise, manifests a marked preference for camp-life. His social instincts are gregarious. It is observed that those who are not engaged on estates, and who are thus free to live as they choose, voluntarily congregate in camps consisting of little huts closely huddled together, often overcrowded and dirty. In this way the Indians in the colony may be said to live apart from the rest of the community, leading an exclusive social life. Although the insanitary state of the camps cannot be accepted as an explanation of the development of an altogether exceptional disease, its spread among a population so circumstanced can be easily understood, while the habits of the people, at once gregarious and exclusive, may have tended to promote its spread amongst themselves, and limited its diffusion among other sections of the community" (26).

XIV.—Sex.

Dr. Lovell states "that the liability of males was about twice that of females"; but that sex *per se* made no difference in incidence, is evident from the further statement that the liability of male and female children was equal. He gives statistics to support these statements; but the number of male and female population from which the figures were collected is not recorded. Dr. Lovell suggests that overwork and exposure may account for the excess of male cases; but it is possible that the comparative seclusion of women was the real cause of the difference. Dr. Nairne also states that men suffered more than women among the South Sylhet coolies (9). This observation is subject to the same criticism. No other observer makes mention of the greater liability of males to contract the disease; and my impression is that I saw as many women as men suffering in my village inspections, and this impression is supported by some statistics which I collected.

XV.—Age.

Dr. Rammay Ray states that the disease was more common between fifteen and sixty than under or over these ages. He met with but three cases under seven years, and none under four years, in 650 cases. Dr. Lovell's testimony is to the same effect (15). "Children under puberty were less liable than men"; and he makes the important statement that "infants at the breast were seldom attacked" (26).

XVI.—State of Health at the Time of Attack.

I have shown that there were many starving, cachectic, anæmic, and scorbutic people living in and about Calcutta during the time that this disease was prevailing, and it would have been a marvel had these escaped attack. Many of them did suffer; but more of them, equally or more seriously affected by the prevailing deterioration of health, did not (Rammay Ray, 15). On the other hand, it is quite certain that persons in excellent health and condition up to the hour of attack were seized suddenly by this complaint. Dr. O'Brien's cases place this point beyond doubt (3); and there is no indication in Dr. Nairne's or Dr. Lovell's reports that the weakly, or emaciated, or otherwise unhealthy,

were more liable to attack than the sound and strong. The disease, though it was a cause of ill-health in its victims, was not the expression, or outcome, or climax of previous constitutional derangement. It is also important to note that prolonged residence in the tainted locality did not seem to be necessary to cause or condition liability to attack.

DIFFUSION.

I now proceed to consider the epidemiological aspects of the outbreak, and these may be displayed under the heads of: (1) Diffusion, in respect of area, density, and rate; (2) Localisation; (3) Grouping; (4) Portability; (5) Communicability; (6) Latency; (7) Immunity.

These heads are practically resolvable into two questions affecting the progression of the malady and the manner and means of progression.

XVII.—Growth and Diffusion of the Disease.

Limiting our study of this question to the three localities, namely, Calcutta, Shillong, and Mauritius, regarding which our information is most complete; and waiving the question of primary origin for the present, there is convincing evidence in each case that the disease, as an epidemic, grew from small beginnings, gradually extending its area, seized increasing numbers, reached a climax, and then waned and vanished. This may be called an epidemic wave. There were three such waves in Calcutta, but only one at Shillong and Mauritius. But the area of diffusion was, as I have shown, exceedingly limited in Calcutta. Each successive wave overstepped the limits of its predecessor, and the whole invasion was confined to a few suburban, and still fewer urban villages. Similarly, at Shillong the disease was confined to the station, and did not extend to the surrounding villages. In Mauritius its diffusiveness was greater, and it rapidly covered several districts one after another. It also affected a larger proportion of the communities among which it broke out. The disease had, in fact, in India, so to speak, a very limited and partial geography, indicating weak diffusibility, and this weakness was also manifested in respect of its incidence over the affected area. Statistics are wanting to show the proportion of seizures in the infected villages, but it is quite certain that sufferers constituted a minority of the home-

stead population. Nor was the rate or speed of diffusion rapid. In Calcutta it took three years to cover the infected area. The rate of diffusion seems to have been more rapid at Shillong, and still more so in Mauritius, with its milder and more equable climate; but both progress and increase of sick were palpably perceptible and measurable in each instance.* In curious contrast with weak general diffusibility was the rapid and complete manner in which the disease sometimes affected whole households and families. Of this I shall give instances later on. The other epidemics of which I have spoken, namely, dengue and influenza, presented a striking contrast in these respects to the disease under consideration. Their invasion was sudden, incidence almost exhaustive, as regards both area and population, progress rapid, and stages of waxing, climax, and waning quickly successive.

XVIII.—Localisation.

In Calcutta the disease appeared to locate itself in particular villages and parts of villages; but, on investigation, this localising was found to be more apparent than real. I ascertained that the disease attacked houses in a village in a promiscuous way, that the affected homesteads were mostly scattered throughout the locality, and not necessarily contiguous (24). Dr. Rammay Ray's experience was to the same effect (15). Dr. O'Brien found that the disease did not confine itself to particular parts of the station of Shillong, but broke out in places widely apart (10). On the other hand, Dr. Lovell found that the disease, when it broke out in one house or camp, spread more or less extensively throughout the neighbouring huts (26). These statements are not suggestive of a community of local influences.

XIX.—Grouping.

The personal element expressed by the term grouping has more evidence in its support than the topical, as suggested by the term localisation, more particularly in Mauritius, where conditions of place and climate seemed to have less influence over its manifestation and progress than in India. Indeed, this mode of prevalence constitutes the most noteworthy phase of the disease, epidemio-

* A special census of a locality in which the disease prevailed gave the following results:—Number of houses, 60; inhabitants, 360; houses attacked, 10; inhabitants in these, 65; attacked, 15; died, 10.

logically considered; the unit group being the family or household, and the composite group, the community of families of the same race, caste, occupation, and habits, associating in domestic intercourse, work, business, friendship, worship, and so forth. This grouping furnishes the key to diffusion and progress. The disease spread among tailors, boatmen, clerks, servants, sepoys, coolies, etc., and limited itself for a time, or altogether, to the class first affected. Dr. Rammay Ray found in Calcutta that "the disease did not affect large masses of people suddenly and at once, but went on gradually attacking family after family, and encroaching upon more extended areas. Only one member or a servant of a family was found to be affected first, and seemed to communicate the disease to almost all the rest, one after the other" (15). Dr. O'Brien at Shillong observes that "the disease appears to have spread after the manner of an epidemic, viz., attacked entire households and families, and spread from such households to the houses of the friends who visited them" (10). Dr. Lovell says, that "when one member of a household took the disease some of the others almost invariably became affected within a few days" (26), and he goes on in the passage to which I have already referred to show how the spread in a camp was similar to that in a household. In some cases the outbreak in a family seems to have been simultaneous; but this may have been more apparent than real, because the disease, as I have shown, commences in different ways, and statements made long after the event, on more or less vague recollection, are not to be very implicitly relied on. Family groups are frequently mentioned in the records on which this paper is founded. I have extracted a few of them.

I. Husband, wife, daughter, and two servants successively (O'Brien, 10).

II. Clerk, cook, and another clerk in same compound successively (O'Brien, 10).

III. Servant, wife, master, grandson, successively (O'Brien, 10).

IV. Seven in a family of 19 Eurasians—two servants, lad of 16, two brothers, mother and daughter, successively (Bowser, 14).

V. Seven men living in the same boat attacked on or about the same day (Cayley, 1).

VI. Eleven members of a household—1. Clerk (1st Dec.); 2. Servant (1st Dec.); 3. Servant (4th Dec.); 4. Daughter (3rd Jan.); 5. Wife (7th Jan.); 6. Servant (9th Jan.); 7. Servant (9th Jan.). 4, 5, 6, and 7 arrived 31st Dec.; 8, 9, 10, 11. Four others (O'Brien, 10).

VII. Master, four children, and servants, successively (O'Brien, 10).

VIII. Bearer and two Hindustani servants. Master (European) escaped (O'Brien, 10).

IX. 1. Adjutant's clerk; 2. Another clerk in same office; 3. Sepoy orderly in same office; 4. Sepoy living close to 3; 5. Wife of a sepoy in same barrack as 3; 6. Wife of 3 (O'Brien, 10).

x. Hospital kahar and another kahar living in same hut (O'Brien, 10).
xi. Five Mahomedans—two daughters, two servants, and an old man (Naylor, 14).
xii. Village cases collected by self.

Number of Inmates.		Number attacked.		Number died.
6	...	3	...	1
11	...	11	...	0
9	...	3	...	1
8	...	7	...	0
7	...	2	...	0
5	...	5	...	2
4	...	4	...	1
8	...	8	...	3
58	...	43	..	8

This list of family groups might be extended.

XX.—Portability.

I use the term portability as indicating the conveyance of the disease, or its cause, from infected to distant uninfected places. The evidence on this point is more inferential than direct; but, taking Calcutta as the headquarters of the disease, there is no other way of reasonably accounting for its subsequent appearance at Dacca, Shillong, and other places in Assam, Cachar, and Sylhet, and in the distant island of Mauritius, than deportation by human beings. Whether these contracted the disease in Calcutta, and were themselves the medium of transference, or whether they conveyed with them some fomes or *materies morbi*, it is impossible to say. The evidence was not taken at the time, and it is vain now to search for it. But, *quantum valeant*, the facts recorded are in favour of the view we have stated. No doubt more complete evidence would be satisfactory; but the probable cannot be rejected because the data are not demonstrative, and to refuse to hold guarded and provisional beliefs in these matters, because exact and demonstrative data are wanting, appears to me to be both unwise and unscientific.

XXI.—Communicability.

The term communicability appears to me to be preferable to the terms contagion or infection; because it simply expresses the fact of transference of the disease from man to man without committing us to a theory of the mode of transference, whether direct or indirect, simple, absolute or conditioned. Opinions differed regarding the infectiousness of the disease, but it is evident that these opinions must depend upon the sense in which the terms infectiousness or

contagiousness are employed. Dr. O'Brien considered the disease contagious, just as measles, scarlatina, or any of the exanthematous fevers are (10). Dr. Kastagir inclined to the same opinion (16). Dr. Lovell states that the great majority of the Mauritius doctors were opposed to a theory of contagion, and himself gives a guarded opinion, remarking that the ways by which a poison may be diffused and transported are so innumerable, and so little understood, and the observations bearing upon the propagation of the disease are so few, that the question of the contagiousness cannot be regarded as finally settled (26). Dr. Rammay Ray argued that the germs of the disease were carried about by people and developed other germs outside of them, affecting others who lived or came in contact with them, and somehow or other imbibed the poison. This is a doctrine of simple conveyance or indirect or mediate communication.

Taking communicability in its widest sense, as indicating that human agency and intercourse constituted in some way or other the means and power by which the disease grew in bulk and spread, there is abundant evidence in favour of it.

1. There is the general evidence rendered by the resemblance of this epidemic to others whose causation is better known.

2. There are the facts already alluded to of the manner in which the disease appeared and spread in a locality and among persons holding close domestic and social intercourse.

3. There are numerous recorded instances in which the disease was apparently introduced into a healthy household by a person sick of the disease.

I. Clerk labouring under disease came to live with another clerk. Cook of latter got ill, then clerk and another clerk living with him, in 7, 10, and 14 days (O'Brien, 10).

II. Prisoner admitted with disease came into close contact with another prisoner in hospital, who got ill (O'Brien, 10).

III. Two children suffering from the complaint were brought to a healthy house, the inmates of which were shortly afterwards seized with it (K. L. Day, 14).

IV. A maid-servant visiting an infected house caught the disease, and within a week all the inmates of the house in which she served, 9 in number, were seized (Harvey, 14).

V. Girl suffering from disease used to visit father's house; three members of the family became affected (Rammay Ray, 15).

4. There are instances of persons visiting infected houses and subsequently contracting the disease.

I. Clerk in the habit of visiting at another clerk's house in which every member of the family had dropsy, and being visited by them; he got ill (O'Brien, 10).

II. Maid-servant in Chuckerbere visited infected house at Ballygunge, and got ill (Harvey, 14).

III. Man-servant of family in Bhowanipore visited a house where disease existed. He got ill, and communicated the disease to six members of his master's family (Rammay Ray, 15).

IV. A Baboo of Bhowanipore caught the disease from Khalassees of Kidderpore, with whom he was brought into contact in business. All the members of his family (two males and two females) were subsequently seized, except young children under six (Rammay Ray, 15).

V. Baboo frequented house of neighbour; he got ill, and then his wife and grandchild (Rammay Ray, 15).

VI. Maid-servant visited infected house, got ill, and six members of master's family were seized, also a coachman (Rammay Ray, 15).

VII. Baboo visited infected house at Ballygunge, got the disease, and his wife and others subsequently suffered from it (Rammay Ray, 15).

5. There are also instances of persons coming to live in infected houses getting ill.

I. Wife, daughter, and two servants came from Dacca to house of a clerk who was ill, together with two servants. All four became affected within a fortnight (O'Brien, 10).

II. Two female attendants who came to nurse sick children fell ill (Rammay Ray, 15).

6. Evidence of direct personal contagion without possible intervention of media is scanty and weak. The case of the two prisoners in the Shillong jail points in this direction, and a strong instance is given by Dr. Clarenc of Moka, in Mauritius, of a coolie (Lutchman) returning from India apparently contracting the disease from a fellow-passenger. Dr. O'Brien's cases would fix the incubation period at from four to fourteen days.

These considerations and cases render it morally certain that human agency was mainly concerned in what we may term the dynamics of the outbreak, and that the disease was somehow transferred from man to man; but in India the small dimensions and slow progress and large margin of immunity which characterised the disease would indicate that the transfer of disease from man to man was encompassed with difficulties, either on account of the difficult conditions of transfer or entry, or the sparing susceptibility or good power of resistance. In Mauritius, on the other hand, the diffusive energy and power of the disease were considerably greater.

XXII.—Latency.

The epidemic in Calcutta manifested in a most signal and rhythmical manner the phenomena of dormancy or latency

and recrudescence. It does not appear whether there were sporadic cases, as in some other epidemics, during the period of dormancy. In Shillong and Mauritius there was only one outbreak, and latency was apparently supplanted by extinction. In Calcutta, latency could not have been due to exhausted pabulum, because the incidence of the disease was so partial, and recrudescence took place in and around its old haunts. The phenomenon can only be attributed to seasonal influences. Even the, so to speak, rampant epidemic of dengue yielded to these, and failed for want of warmth to reach high altitudes or latitudes; it was stayed in its course by the cold of October in Upper India. Even influenza in Calcutta had a period of dormancy after sweeping over the town in 1890, and a partial recrudescence in 1891. One great contrast existed between these three epidemics, in that cold and humidity seemed to favour the dropsical disease, while heat and dryness were more congenial to dengue and influenza. It is important to note, however, that in Mauritius the origin and spread of the disease took place under conditions of drought and warmth.

XXIII.—Immunity.

That the disease was not a very catching one is indicated by many observations. Medical attendants escaped it. It did not spread in either of the four hospitals which admitted cases. People visited tainted houses without getting the disease, or, having contracted it, returned to their native villages without imparting it. Neither places nor persons seem to take it very readily. The diffusibility was weak and communicability slight.* It was this frequent escape after exposure to infection which led many to doubt the infectious nature of the disease. Taking the disease as a whole, its incidence, even in the worst villages in Calcutta, was very partial, and the margin of exemption very large. This does not necessarily militate against a doctrine of diffusion by human agency and intercourse. All epidemic diseases have a margin of immunity. Even dengue and influenza were far from exhaustive, however small and self-contained the community—regiment or jail, for example. In the absence of positive knowledge regarding the exciting or proximate cause of the malady, speculation regarding

* These statements refer more to India than Mauritius, where, under different circumstances of climate and population, the diffusion of the disease was stronger.

the degree of incidence or immunity is unprofitable; but it is safe to aver in this case that personal susceptibility is a less satisfactory explanation than difficulties of transference, due to the nature or conditions of activity of the *materies morbi.*

XXIV.—Origin and Causation.

Under this head I may briefly sum up all that is known regarding the appearance and spread of this disease as systematically detailed in the preceding sections. How it sprang up in Calcutta for the first time in October 1877, it is impossible to say. Dr. Rammay Ray believes that it was imported from the Madras Presidency by famine fugitives, or traders. He states that, when on famine duty in the Presidency of Madras, he saw some 500 cases of this disease, which, on his return to Calcutta in January 1879, to resume his duties in the centre of the affected area, he had no difficulty in recognising and identifying as the same disease (15). He writes of "its occurrence in Calcutta after the advent to it of some of the famine-stricken people from Madras, and the establishment of a freer intercourse between the people of both places, especially among merchants." Whether this is the truth as regards the origin of the disease in Calcutta or not, it is extremely difficult to say. No other explanation has been given, and none can now be found. But, accepting Calcutta as the starting-point of the disease, its appearence elsewhere is more reasonably explained by a theory of communication by personal agency or intercourse, than by a theory of *de novo* origin in the instance of each outbreak or case. Dr. O'Brien surmises that the disease was imported from Dacca, but he also shows that persons arrived from Calcutta before the disease broke out, in whose persons and families it subsequently made its appearance (3-10). Dr. Lovell was unable to obtain positive evidence of importation, but he shows that there was no lack of opportunity, for ten vessels carrying Indians arrived in Mauritius between the 11th of August and 8th of November 1878, that the appearance of the disease in Mauritius was consecutive to its existence in Calcutta, and that vessels embarking coolies depart from the place (Garden Reach) when the disease appeared first and lingered longest in Calcutta. He also shows that one man was actually seized on board ship, from intercourse with a man who had previously contracted the disease in India. This was, however, some time after the disease had broken out in Mauritius.

On the whole, leaving the question of original generation as unknown and unknowable, the facts which have been recorded justify us in considering this a communicable disease, but communicable under conditions, seasonal and otherwise, which rendered its diffusion difficult and tardy, and resulted in its extinction after a partial incidence over a comparatively limited area.

The disease, in short, presents an epidemic rather than an endemic facies, and, as shown by Smith, Harvey, Rammay Ray, O'Brien, and Lovell, all reputed causes connected with soil and season, insanitary surroundings, starvation, and constitutional defects or depravities, fail in the light of experience to account for the outbreak. Negative evidence with reference to alleged factors has a different, stronger, and more conclusive value than in regard to the question of communicability. Mere absence of communication, when apparent opportunity existed, by no means disproves communication in other instances. But absence of a factor such as preceding ill-health, malarious disease, anæmia, or scurvy, in any one case, indicates that such a condition is not a necessary precursor or essential cause, and when the absence is observed in many cases, the argument gains in strength. The parallel demonstration as regards communicability would be the citation of an instance of appearance of the disease without the possibility of direct or indirect communication with a person or persons similarly affected. No such instance was observed or recorded in this epidemic.

XXV.—Pathology and Identification.

The disease which I have described was, to employ Farre's familiar nomenclature, zymotic, and not enthetic—an affection due to some poison working in the blood and system, rather than a symptom or outcome of previous ill-health, general or special. The dropsy cannot, I think, be regarded as an anæmic dropsy. It occurred too suddenly, and in persons previously in perfect health, and was associated with active symptoms such as fever, rash, vomiting, and diarrhœa, which are not generally associated with anæmic dropsy. The effusion was mainly cutaneous and subcutaneous, resembling some forms of erythema and erysipelas, and the acuter cases of elephantiasis fever, and though the effused fluid was influenced by gravitation, this was evidently a minor and secondary condition of accumulation, for it was found in some cases in the upper

parts of the body in early stages of the disease. The effusion was not confined to the skin and subcutaneous areolar tissue, but occurred in all the tissues of the body and into the cavities—the preference being apparently in the order stated. The cutaneous effusion, however, was evidently a more active and acute process than the internal effusions. The nervous centres were not specially or severely subject to the process, and the peritoneum was less prone to be filled than the chest cavities. Indeed, the absence of ascites, even when the abdominal parietes were filled to hardness with fluid, was an undoubted and most remarkable fact. Nor can the dropsy be looked upon as a sequela similar to scarlatinal dropsy. It was often the earliest and sometimes the sole symptom. Whether it was due to disorder of the innervation of vessels, or to disturbance of adjustment between the vessels and tissues, or to perverted action of the lymphatics, or a change in the physical state of the blood, I am unable to say. The observed excess of leucocytes and germinal material in the blood points to irritation of the blood-making glands and textures. I incline to the belief that the disease was really an exanthematous fever, the dropsy constituting a phenomenon homologous to the eruptions of such diseases.

I have hinted at an analogy with some of the acuter forms of elephantiasis fever, but the differences are too many and profound to justify more than the suggestion of analogy. Nor do the nature and course of the disease warrant any suspicion that it was due to any intestinal parasite, similar to that which has been found in Ceylon and Assam to be associated with or productive of anæmic and cachectic states, frequently terminating in dropsical effusions.

The question now remains, What was this disease? Was it a new form of disease, or was it the disease previously known and described as Beri-beri? On this subject there has been a considerable diversity of opinion. I shall endeavour to place the issues before you as briefly and clearly as I can. Three classes of medical men have recorded opinions, namely: 1st. Those who had personal experience both of the present disease and of that recognised as beri-beri; 2nd. Those who had personal experience of the present disease, but none of the other; and 3rd. Those who knew beri-beri from experience or study, but had not seen any case of this disease.

To the first class belong Drs. Rammay Ray, Harvey, and Coates. Dr. Rammay Ray, while on famine duty in Madras,

had seen 500 cases of what was called beri-beri there, and on returning to India saw at least 150 cases of the Calcutta disease, and had no hesitation in pronouncing them to be the same. Granting that they were the same disease, the question arises, Was it genuine and veritable beri-beri that Dr. Rammay Ray (15) saw in Madras, or some new, and in some respects similar, famine fever? I incline to think that this latter surmise is correct. Dr. Harvey (14) had also been on famine duty in Madras, and had seen beri-beri at Berar and Cadapah, as also in Central India and Rajputana. He had very little doubt that the Calcutta disease was the same, but remarks, significantly, that "the one (the beri-beri of Marshall and Hamilton) is exceedingly chronic, and the swelled feet appear at the end of a long train of symptoms; the other (the Calcutta disease) is at first essentially acute, and the swelling is often the earliest symptom." Dr. Coates had seen beri-beri among Madras sepoys at Cuttack, and also cases of the Calcutta disease, and they did not appear to him to be the same disease (19). He considered the Calcutta and Mauritius disease to be the same (21).

To the second class belong Drs. O'Brien, Lovell, and Davidson. Dr. O'Brien (10), after citing Morehead's description of beri-beri, and showing that, according to his experience in Shillong, neither cold and damp, nor poverty and starvation, nor scurvy, nor malaria, nor debility, could be accounted causes, arrived at the conclusion that he had to deal with a new and distinct contagious disease. This conclusion is all the more important in that he was at first inclined to consider the disease to be beri-beri.

Dr. Lovell (26), after stating that he considered the dropsy to be due to anæmia, and the anæmia to a poison or miasm of some kind entering the system, and acting directly upon the blood, or indirectly through the blood glands, and after citing the various and somewhat discordant descriptions of beri-beri given by different authors, points out the absence of numbness and paralysis, the small mortality, the presence of fever and rash, as well as the absence of previous ill-health, the sudden attack and complete recovery. In the Mauritius disease he arrives at the conclusion that "acute anæmic dropsy is a disease *sui generis;* not due to malaria, and not identical with beri-beri." After perusing the Calcutta reports, he considered the disease which prevailed there to be identical with the Mauritius disease. Dr. Davidson takes the same view of the disease and epidemic as Dr. Lovell.

To the third class belong Drs. Cornish, Chevers, Fayrer, and Moore.

Surgeon-General Cornish, after a study of the records of the Calcutta and Mauritius outbreaks, was "quite satisfied that the disease described in these reports was not the beri-beri endemic in the northern districts on the eastern coast of the Madras Presidency, in which disease the staggering gait and disordered nervous sensations are the most prominent features" (26). Dr. Norman Chevers, after carefully studying the facts of the Calcutta and Mauritius outbreaks in the light of the literature of beri-beri, with which he was intimately acquainted, concluded that the malady was an exanthematous fever, and that the dropsy was to be looked on as a sequela. Seeing, however, that the dropsy was in some cases the first, and in all a very early symptom of the attack, I can hardly consent to its being called a sequela. He proposed, however, to retain the name beri-beri, or beri-beri fever, notwithstanding that he indicated that it has been applied to four other conditions differing gravely from each other in etiology and pathology, and agreeing only in the presence of paralysis and dropsy (27). In a paper read before the Medical Society of London on the 31st of March 1884 (see *Lancet*, vol. i, of 1884, page 612), Dr. Chevers proposed the name of *Febris exanthematosa Orientalis* for the disease. To this I hold a strong objection: 1st, because the exanthem was by no means an invariable or even frequent symptom of the disease. Dr. O'Brien never met with it at Shillong, and it was rare in Calcutta; 2nd, because, when it did appear, it either accompanied or followed the dropsy, and never preceded it; and 3rd, because if the Brazil epidemics are the same as that which I have described, the term *Orientalis* is obviously inapplicable. Sir Joseph Fayrer had also made a careful study of this outbreak as it appeared in Calcutta and Shillong, and of previous and subsequent writings regarding beri-beri, and he was quite inclined to pronounce the disease to be beri-beri, which, occurring sporadically in Bengal, assumed an epidemic condition, and in consequence presented novelties in its symptoms and phenomena (28). More recently, Sir Joseph Fayrer was inclined to take the same view of the disease as Dr. Chevers (see *Lancet, loc. cit.*). Sir William Moore, who had experience of beri-beri in various parts of India, and had studied the Calcutta and Mauritius reports, believes that the disease which prevailed then was beri-beri, and that beri-beri is a form of scurvy (29).

CONCLUSION.

It would prolong this already lengthy paper unduly were I to enter on a discussion of that protean malady, beri-beri, with the literature of which I have pretty fully acquainted myself, or to refer to other epidemics of dropsy which have been described as prevailing in Brazil and elsewhere. I believe that the term beri-beri has been applied to a number of different diseased conditions, and that, as these conditions are investigated and identified, and their true pathology and causation ascertained, the term will disappear from medical nomenclature. I submit that the disease which I have described would be more fitly designated epidemic dropsy, and I venture, by way of conclusion, to offer the following concise definition of it.

Epidemic Dropsy.—A specific disease, characterised by the sudden appearance of anasarca, preceded in most cases by fever, vomiting, diarrhœa, or irritation of the skin; often accompanied by a rash, by fever of a mild remittent type, and disorder of the bowels; the urine varies in quantity, colour, and frequency, is very rarely albuminous, and never suppressed; deep-seated pains in the limbs and dyspnœa are very common; anæmia, which is apt to be progressive, is a prominent and constant feature of the disease; œdema of the lungs, and distension of the pleuræ and pericardium frequently occur in the later stages; the attack lasts from three to six weeks; the mortality varies from 2 to 40 per cent., according to circumstances; death is usually caused by lung and heart complications, and is sometimes early and sudden. The disease is communicable from person to person, and portable by human agency and intercourse; but its diffusion is feeble, and depends on seasonal and other conditions which modify its epidemic vitality and restrict its extension and transmission.

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POST-SCARLATINAL DIPHTHERIA:

A Statistical and Etiological Study.

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Hon. Treasurer of the Society.

(*Read: February 15th*, 1893.)

Mr. President and Gentlemen,—I am anxious to lay before the Society, both as a permanent record and as a basis for discussion, some facts relating to the occurrence of post-scarlatinal diphtheria in the several fever hospitals of the Metropolitan Asylums Board. The subject possesses an importance which is not confined to its academic or scientific aspect, but extends into considerations of practical administration, as well as the more sentimental view points of the lay public. By post-scarlatinal diphtheria is meant simply and briefly true diphtheria occurring during scarlatinal convalescence. I do not include membranous exudation on the fauces during the acute stage, often seen in scarlet fever. That patients recovering from one infectious disease should contract another, often with fatal issue, is at all times an undesirable occurrence, and distressing alike to hospital authorities and to patients' friends. This, unfortunately, is sometimes an inevitable accident in hospital administration: but in such cases the reason for the accident is usually to be quickly discovered in some more or less obvious channel of infection. But when no such source is distinctly forthcoming, it behoves practical epidemiologists to endeavour so to sift the facts as to obtain, if possible, some grain of scientific truth amongst them. With this object, and with the hope that those around me will give their assistance by contributing fully to the discussion which will ensue, I have analysed the reports and returns of the Asylums Board hospitals which bear upon the subject I have introduced.

Until the end of the year 1888 these hospitals admitted only scarlet and enteric fevers; some of them having, in addition, a few typhus beds. But at the end of 1888 a new departure was witnessed in the reception of diphtheria, 50 beds being set apart for that disease at the Eastern Hospital,

TABLE A.—*Showing the Incidence of Post*
of the Asylums Board

Year.	Eastern.		Wester	
	Scarlet Fever.	Post-Scarlatinal Diphtheria.	Scarlet Fever.	Sca Dip
1884	618	nil	124	
1885	899	1*	239	
1886	702	2†	343	
1887	1104	nil§	609	
1884–87 ...	3323	3	1315	

TABLE B.—*Showing the Incidence of Po sylums*
Board during the four

Year.	Eastern.				
	Scarlet Fever.	Post-Scarlatinal Diphtheria.	Deaths from Latter.	Inc per	Case Mortality.
1889	620	24	Not recorded.		73.6
1890	654	40	,,		85.6
1891	603	32	,,		46.6
1892	965	22	15		66.6
1889 to 1892	2842	118	† 15		70.8
Year.	North-Western.				
1889	581	11	8		
1890	1069	23	10		
1891	1079	27	13		
1892	1347	25	8		
1889 to 1892	4076	86	39		

* Excluding the

20 at the Western, 22 at the South-Eastern, and 44 at the North-Western. (These 136 beds were increased in 1889 to 221, reduced in 1890 to 163, again increased in 1891 to 204, and in 1892 to 263.) Let us inquire into the incidence of post-scarlatinal diphtheria at the several hospitals before and after this admission of diphtheria at the end of 1888.

Table A (appended) shows the incidence of diphtheria on completed cases of scarlet fever at five of these hospitals during the four years 1884-87, before diphtheria was received. It will be seen that during the four years mentioned, 3 cases occurred at the Eastern Hospital amongst 3,323 cases of scarlet fever; 12 at the Western amongst 1,315; 5 at the South-Eastern amongst 1,771; none at the South-Western amongst 1,305; 4 at the North-Western amongst 880. The total incidence in those years was 24 cases amongst 8,594 cases of scarlet fever, a percentage incidence of 0.2 (32 cases of what was apparently simple laryngitis are not included herein, as no evidence of their diphtheritic nature is recorded; if they are reckoned as diphtheritic, the total incidence per cent. becomes 0.6). As regards the 12 cases at the Western Hospital, 5 of them developed within a week of admission, and 3 within a fortnight; so that at least 8 were related to the acute stage of scarlet fever, and can hardly be reckoned as post-scarlatinal.

Table B (appended) shows the incidence of diphtheria on completed cases of scarlet fever at five of the hospitals during the four years 1889-92, after diphtheria was received, with its case-mortality. It will be seen that during these four years the Eastern Hospital had 118 cases of post-scarlatinal diphtheria amongst 2,842 cases of scarlet fever; there is no record, however, as to fatality, except in 1892, when 15 out of 22 died. The Western Hospital had 91 cases amongst 1,628, of which 65 died, a percentage incidence of 5.5, and case-mortality of 71.4. These were each greater in 1890 than in any other year. The South-Eastern Hospital had 72 cases amongst 2,498, of whom 51 died, a percentage incidence of 2.8, and a case-mortality of 70.8. The North-Western had 86 cases amongst 4,076, of whom 39 died, an incidence of 2.1 per cent., and a case-mortality of 45.3. The total incidence was 367 on 11,044 cases of scarlet fever, of whom 170 died (excluding the unknown fatality at the Eastern Hospital), giving an incidence of 3.3 per cent., and a case-mortality of 46.3 (neglecting the unknown fatality of 96 cases at the Eastern Hospital in 1889-91). The incidence was fairly uniform during the four years, though there was a distinct excess in 1890. The comparative

fatality in the different years cannot, of course, be determined on account of the absence of record at the Eastern Hospital. The percentage incidence of post-scarlatinal diphtheria was greatest at the Western, and least at the North-Western Hospital. The case-mortality, too, was much lower at the North-Western than at either the Western or South-Eastern. This minimum incidence and fatality at the North-Western Hospital may perhaps be not unrelated to the fact that from the North-Western Hospital fewer cases are transferred to convalesce at other hospitals of the Board than from the other "acute" hospitals, and that consequently there is at that hospital less aggregation of acute cases than at any other hospital. Thus, during the four years 1889-92, the proportion of cases transferred to the total discharged was, from the North-Western 27 per cent., compared with 41 per cent. at the South-Eastern, and 64 per cent. at the Western Hospital. (I might allude here to a special report, issued in February 1889, in which I showed that the incidence of "throat illness" amongst scarlet-fever patients at the Western Hospital had been doubled, and its fatality increased one-fourth, since the system of drafting convalescent cases away had been established.) It is also worthy of notice that the proportion of diphtheria convalescents transferred to the total discharged was higher at the Western and Eastern Hospitals during 1889-91 than at the South-Eastern and North-Western. For the percentage proportions were, for the Western 55, for the Eastern 49, for the South-Eastern 13, and for the North-Western 0.8. These proportions tally in order, though not altogether in degree, with the order of percentage incidence of post-scarlatinal diphtheria at each hospital in 1889-92, given in Table B, viz.:—Western 5.5, Eastern 4.1, South-Eastern 2.8, North-Western 2.1. It is noteworthy that the hospitals which send away most of their scarlet fever and diphtheria convalescents, and therefore retain in their wards the greatest number of both these diseases in the acute stage, have exhibited the greatest amount of post-scarlatinal diphtheria.

In comparing the incidence of post-scarlatinal diphtheria before and after the admission of diphtheria into the "acute" hospitals of the Board, I have omitted the year 1888, inasmuch as diphtheria was first received into these hospitals at various periods at the end of that year, and I am unable to differentiate from the records of the Board, except in one case, between the incidence in 1888, before and after the reception of diphtheria. The numbers for that year are the following:—

Eastern Hospital.—No cases	amongst	830	completely treated	
South-Western.—	„	361	„	
North-Western.—Three	„	923	„	or 0.3 p. c.
South-Eastern.—Seven	„	423	„	or 1.6 p. c.
Western.—Twenty-two	„	332	„	or 6.6 p. c.

Total, 32 amongst 2,869, or 1.1 per cent.

Of the 22 cases at the Western Hospital, only one occurred after the reception of diphtheria; but 11 of the other 21 occurred during the acute pyrexial stage of scarlet fever; and 3 are to be explained by personal infection in the wards, leaving only 7 true post-scarlatinal cases unaccounted for, thus reducing the incidence at that hospital to only 2.2 per cent., and the total incidence of all the hospitals to 0.5 per cent.

I will now proceed to summarise the behaviour of post-scarlatinal diphtheria at each of the "acute" hospitals at which it occurred during 1889-92, noting the time of its occurrence after admission with scarlet fever, the age, the number of wards attacked, and any other important facts given in the Superintendent's reports.

1889.

Eastern Hospital.—Twenty-four cases amongst 620, or 3.8 per cent. No details given.

Western.—Twenty-seven cases amongst 445, or 6.0 per cent.; 18 fatal; case-mortality, 66.6. *Time after admission:* 3 days to 141 days; 7 within a week; 11 from one to four weeks; 9 over four weeks. *Age:* 14 months to 26 years; $\frac{19}{27}$ of the cases and $\frac{15}{18}$ of the deaths under five years. *Wards:* 6 attacked; 7 cases in one ward, but 5 of these attacked within a week of admission. The scarlet-fever ward next the diphtheria ward had fewer cases than two others further off. Membrane found on the soft palate, tonsils, uvula, epiglottis, vocal cords, trachea, large and small bronchi.

South-Eastern.—Nineteen cases amongst 695, or 2.7 per cent.; 14 fatal, or 73.6. *Time after admission:* 1 day to 91 days; 7 under one week; 5 from one to four weeks; 7 over four weeks. *Age:* 2 to 15 years; $\frac{9}{19}$ of the cases under 5, and $\frac{6}{14}$ of the deaths. *Wards:* 7 attacked; 8 cases in one ward, 6 in another, but these wards did not

differ materially from the others. Ward inter-infection accounted for 4 cases. The varieties of diphtheria noticed comprised membranous laryngitis, as well as faucial and laryngeal diphtheria and croup.

North-Western.—Eleven cases in 581, of whom 8 died; percentage incidence, 1.8; case-mortality, 72.7. *Time after admission:* 1 week to 8 weeks; 2 from 1 to 4 weeks; 9 over 4 weeks. *Age:* 2 to 13 years; $\frac{7}{11}$ of the cases and $\frac{6}{8}$ of the deaths under 5.

Summary of 1889.

$\frac{25}{55}$, or 45.4 per cent. of the cases attacked over four weeks after admission. $\frac{35}{55}$, or 63.4 per cent., and $\frac{27}{40}$ of the deaths, or 67.5 per cent., under 5 years of age.

1890.

Eastern Hospital.—Forty cases amongst 654, or 6.1 per cent. No details.

Western.—Thirty-two cases amongst 460, or 7.8 per cent., of whom 25 died, or 78.1 per cent. (High mortality probably due to the fact that 7 of these had measles concurrently or just before, of whom 6 died). *Time after admission:* 6 days to 80 days; 2 under 1 week; 11 from 1 to 4 weeks; 19 over 4 weeks. *Age:* 14 months to 8 years; $\frac{25}{32}$ of the cases and $\frac{22}{25}$ of the deaths under 5 years. *Wards:* 7 attacked; 10 cases of the 32 in the ward next the diphtheria ward, but 4 of them due to inter-infection, as well as 3 in other wards. Membrane was found in the trachea, larynx, and bronchi, and in two cases extended "from the respiratory tract to the bronchi". One case had general paralysis.

South-Eastern.—Twenty-one cases amongst 474, or 4.4 per cent., of whom 18 died, or 85.6 per cent. *Time after admission:* 12 days to 83 days; 7 from 1 to 4 weeks; 14 over 4 weeks. *Age:* $\frac{11}{21}$ of the cases (52.3 per cent.) and $\frac{8}{18}$ of the deaths (44.4 per cent.) under 5 years. *Wards:* 9 attacked; 2 wards had each 5 cases, but 3 of these due to ward inter-infection.

North-Western.—Twenty-three cases amongst 1,069, or 2.1. per cent., of which 10 died (43.4 per cent.). *Time after admission:* 5 days to 11 weeks; 1 under a week, 7 between 1 week and 4, 15 over 4 weeks. *Age:* 13 months to 21 years; $\frac{11}{23}$ of the cases and $\frac{9}{10}$ of the deaths under five years. *Wards:* nine attacked; six in one ward. Four cases due to ward inter-infection. The

varieties of diphtheria noticed were faucial, nasal, pharyngeal, and laryngeal.

Summary of 1890.

$\frac{48}{76}$, or 63.1 per cent. of the cases attacked over four weeks after admission; $\frac{47}{76}$ of the cases and $\frac{29}{53}$ of the deaths under five years, being 61.8 and 54.7 per cent. respectively.

1891.

Eastern Hospital.—Thirty-two cases amongst 603, or 5.1 per cent. No details.

Western.—Fourteen cases amongst 382, or 3.6 per cent., of whom 10 died, or 71.8 per cent. *Time after admission:* 8 days to 39 days; 12 from one to four weeks; 2 over four weeks. *Age:* 2 to 14 years; $\frac{5}{14}$ of the cases and $\frac{7}{10}$ of the deaths under five years. *Wards:* six attacked; the two wards which had the most cases were the furthest distant from the diphtheria wards, and on the opposite side of the hospital. Most of the cases laryngeal; one had palatal paralysis.

South-Eastern.—Seventeen cases amongst 667, or 2.5 per cent., of which 9 died, or 46.6 per cent. *Time after admission:* 12 days to 87; 7 from one to four weeks; 10 over four weeks. *Age:* $\frac{7}{17}$ of the cases (41.1 per cent.) and $\frac{5}{9}$ of the deaths (55.5 per cent.) under 5 years. *Wards:* six attacked; one ward had four cases. (Here and in other cases any slight ward-excess could not be found attributable to any local ward condition.) Of the 7 females who were attacked, 4 had vaginitis as a complication.

North-Western.—Twenty-seven cases amongst 1,079, or 2.5 per cent., 13 fatal, or 48.1 per cent. *Time after admission:* 5 days to 10 weeks; one under a week; 11 from one week to four; 15 over four weeks. *Age:* 14 months to 22 years; $\frac{13}{27}$ of the cases and $\frac{9}{13}$ of the deaths under 5 years. *Wards:* nine attacked; eleven in one ward, eight in another. Seven cases due to ward inter-infection. Faucial diphtheria chiefly noticed.

Summary of 1891.

$\frac{27}{58}$ of the cases, or 46.5 per cent., attacked over four weeks after admission.

$\frac{25}{58}$ of the cases, or 43 per cent., and $\frac{21}{32}$ of the deaths, or 65.6 per cent., under five years of age.

1892.

Eastern Hospital.—Twenty-two cases amongst 965, or 2.2 per cent., of whom 15 were fatal, or 68.1 per cent. (Measles was a complication in 6 of these.) *Time after admission:* 5 days to 60 days; one under one week; 11 from one week to four; 10 over four weeks. *Age:* 8 months to 13 years; $\frac{13}{22}$ of the cases and $\frac{12}{15}$ of the deaths under 5 years. *Wards:* ten attacked; one ward had five cases and another four. Two cases due to ward inter-infection.

Western.—Eighteen cases amongst 395, or 4.5 per cent.; 12 died, or 66.6 per cent. *Time after admission:* 9 days to 76 days; 8 from one to four weeks; 10 over four weeks. *Age:* 13 months to 29 years; $\frac{9}{18}$ of the cases and $\frac{8}{12}$ of the deaths under 5 years. *Wards:* nine attacked; five in the ward furthest from the diphtheria ward; four in the ward nearest the diphtheria ward. $\frac{7}{18}$ of the cases were laryngeal.

South-Eastern.—Fifteen cases amongst 662, or 2.2 per cent.; 10 fatal, or 66.6 per cent. *Time after admission:* 12 days to 86 days; 9 from one to four weeks; 6 over four weeks. *Age:* 2 to 21 years; $\frac{6}{15}$ of the cases and $\frac{5}{10}$ of the deaths under five years. *Wards:* seven attacked; one ward had five cases. Two cases complicated with measles and one with whooping-cough; all these died.

North-Western.—Twenty-five cases amongst 1,347, or 1.8 per cent.; 8 fatal, or 32 per cent. *Time after admission:* 10 from one to four weeks; 15 over four weeks. *Age:* $\frac{7}{25}$ of the cases and $\frac{4}{8}$ of the deaths under 5 years. *Wards:* eleven attacked; one ward had 7 cases, but 2 of these due to ward inter-infection, as well as 2 in another ward, 4 in all. The majority ($\frac{14}{25}$) of the cases were faucial diphtheria.

Summary of 1892.

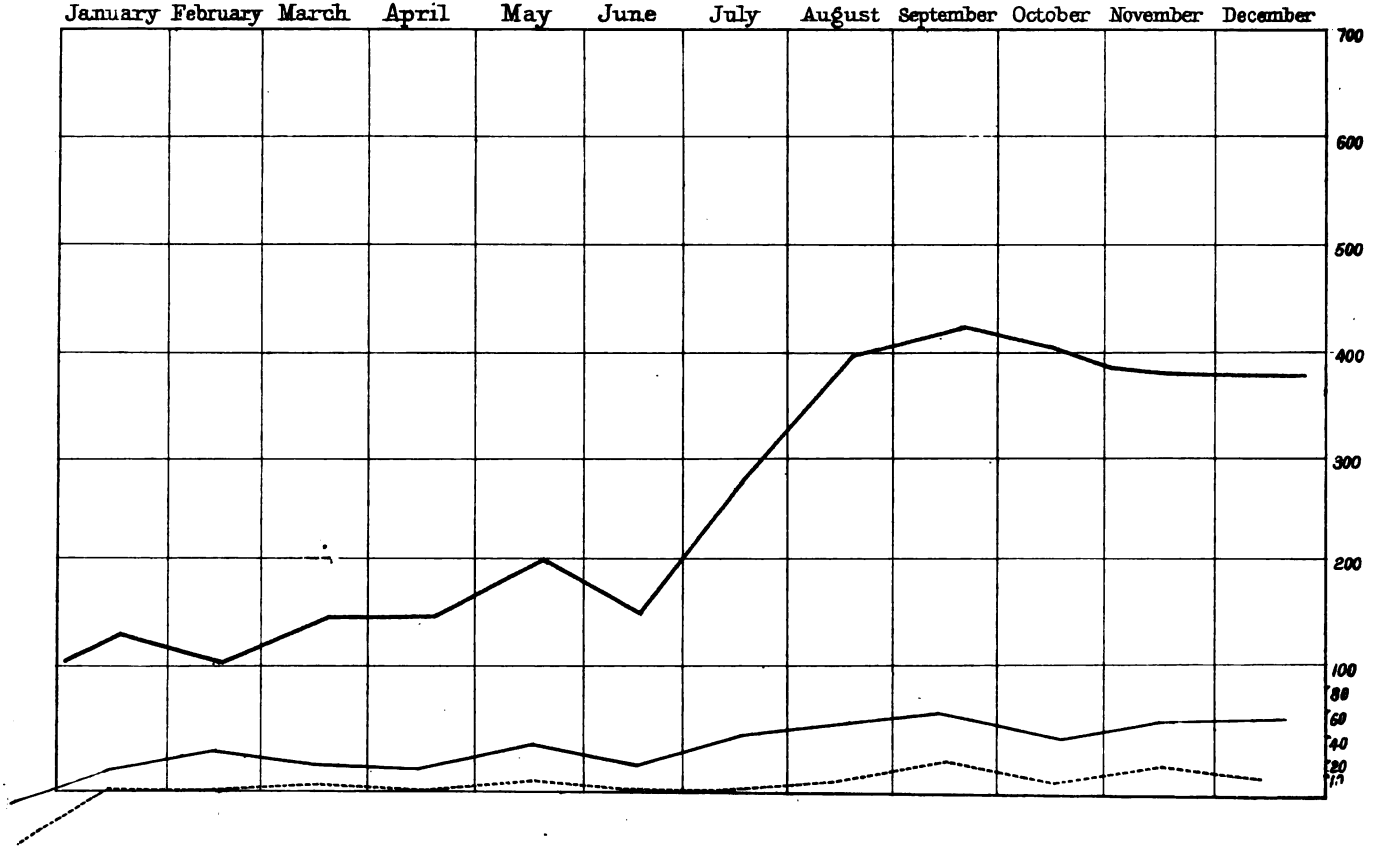
$\frac{41}{80}$ of the cases (51.2 per cent.) attacked over four weeks after admission. $\frac{35}{80}$, or 43.7 per cent. of the cases, and $\frac{29}{45}$, or 64.4 per cent. of the deaths, under five years.

General Summary of the "Acute" Hospitals (1889-92).

$\frac{141}{271}$ of the cases in which details are given were attacked more than four weeks after admission, or 52.0 per cent.; $\frac{111}{271}$ were attacked from one to four weeks after admission, or 40.9; the remainder (7.1 per cent.) were attacked within one week, and might therefore have been incubating the disease when admitted. *Thus post-scarlatinal diphtheria is*

1889. (WESTERN, SOUTH-EASTERN AND NORTH-WESTERN HOSPITALS)

CURVE OF MONTHLY ADMISSIONS OF SCARLET FEVER (RED) & OF DIPHTHERIA (BLACK): WITH THAT OF THE MONTHLY INCIDENCE OF POST SCARLATINAL DIPHTHERIA. (DOTTED LINE).



emphatically a matter of late convalescence. Of these 271 cases, only 38 can be considered to have taken post-scarlatinal diphtheria by personal infection in the wards, leaving 233 unexplained on this hypothesis.

As regards *season of year*, the following was the quarterly incidence of post-scarlatinal diphtheria on the admissions of scarlet fever during 1889-92:—

1*st quarter*,	2.5	per cent.	showing that the incidence was lowest in the third quarter, when scarlet fever is usually at its maximum prevalence.
2*nd* „	1.7	„	
3*rd* „	0.9	„	
4*th* „	1.3	„	

With regard to *age*, $\frac{137}{271}$, or 50.5 per cent. of the cases, and $\frac{116}{170}$, or 68.2 per cent. of the deaths, were under five years of age. This double concurrence of disproportionate incidence and fatality in the first quinquennium of life points to the true diphtheria nature of post-scarlatinal diphtheria, and against its being a mere phase of scarlet fever. For the latter, though showing, like diphtheria, its maximum fatality in the first five years of life, effects its greatest incidence of attack in the second quinquennium, whereas diphtheria attacks and kills disproportionately from 0-5 years.

No sufficient data of sex-distribution were at hand.

I now present to you curves, respectively, of scarlet fever monthly admissions, diphtheria monthly admissions, and of post-scarlatinal diphtheria monthly incidence, at certain of the "acute" hospitals of the Board during each of the four years 1889-92.

It will be first noticed that neither the diphtheria curve nor the post-scarlatinal diphtheria curve bears, except in 1889, any direct relation in any year to that of scarlet fever. The maximum for each was attained in September. This was not repeated in 1890, when the maximum for scarlet fever was again in September, whereas the maxima of the two others occurred in November; the minima being respectively in February, April, and May, for the three diseases. In 1891 the maximum for scarlet fever was three in October, the minimum in June, whilst for diphtheria the maximum was in September and the minimum in January.

In 1892, a year of exceptional prevalence of scarlet fever, a high maximum of that disease occurred in August; but the maxima of diphtheria and post-scarlatinal diphtheria were, respectively, in October and June. The minimum of scarlet fever was in February, the minimum of diphtheria

in the same month, and that of post-scarlatinal diphtheria in April.

But a somewhat greater correspondence (though not a very complete or definite one) is seen between the curves of diphtheria and post-scarlatinal diphtheria. This is more marked in 1889 and 1892 than the other two years, the curves in those years following each other pretty closely, although in the latter year the post-scarlatinal diphtheria curve appears to precede and anticipate the diphtheria curve. In 1890, though the maxima of the two correspond, yet from February to May a distinct inversion is to be observed. In 1891 this inversion is more marked.

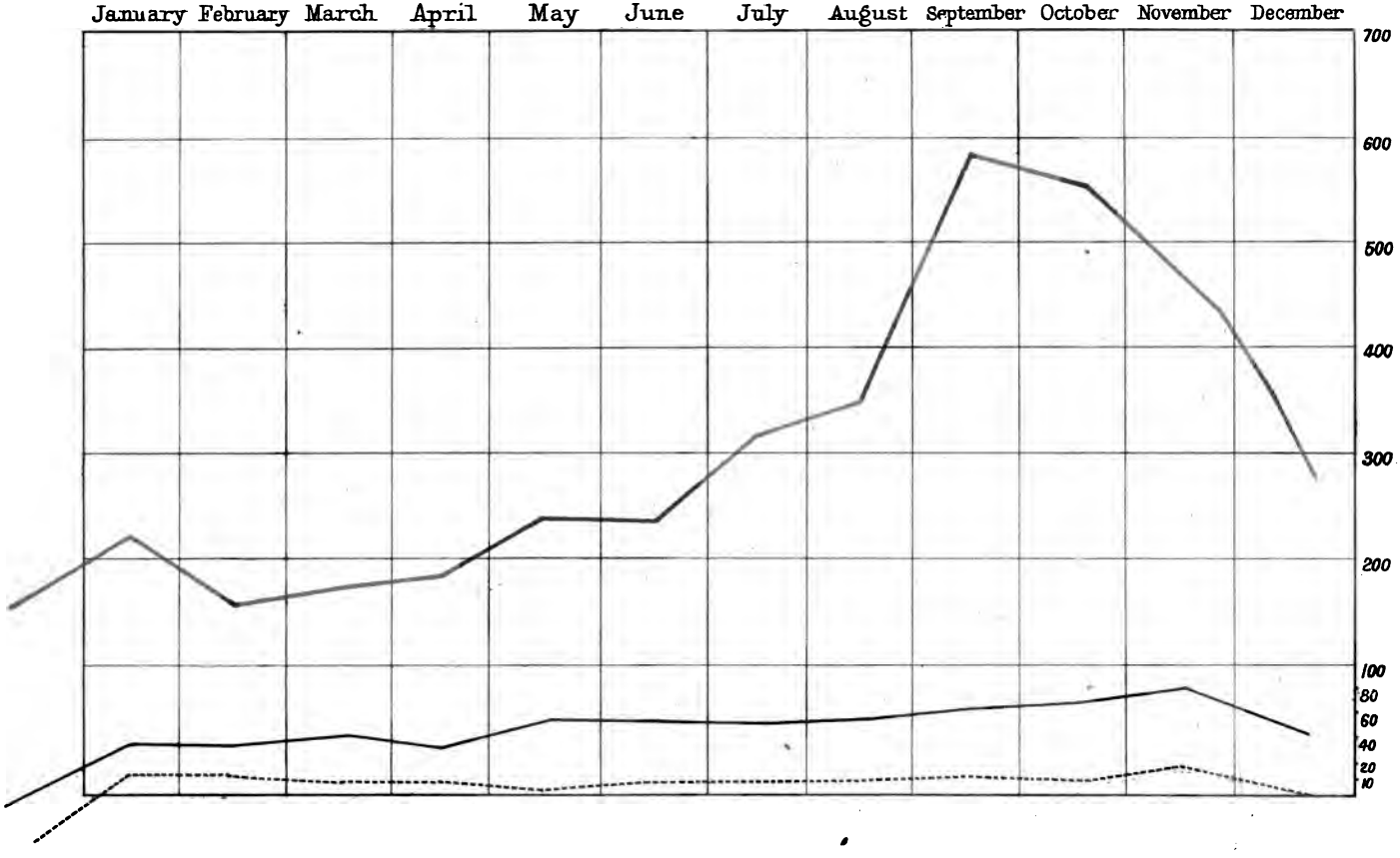
The general indication of these curves, taken as a whole, is, that the complication or sequela of post-scarlatinal diphtheria is more closely related to diphtheria than to scarlet fever, thus confirming the other statistical evidence.

The South-Western Hospital remains to be spoken of separately from the other "acute" hospitals of the Board. It will be perceived from Table A that no post-scarlatinal diphtheria occurred (or, at any rate, was recorded) there during 1884-87 amongst 1,305 scarlet fever cases treated; neither was this the case in 1888, with 361 completely treated scarlet-fever cases. The same absence of post-scarlatinal diphtheria occurred in 1889; but there were only 240 scarlet fever admitted, viz., from October 16th to end of the year, and no diphtheria at all. In 1890 no post-scarlatinal diphtheria occurred amongst 696 completed cases of scarlet fever. But diphtheria was admitted only after the first week in December, and in all only 14 cases were admitted. Almost the same immunity from post-scarlatinal diphtheria occurred at this hospital during 1891, only one case having been noticed amongst the 768 cases of scarlet fever treated, although 211 cases of diphtheria were admitted during the year—a higher total than at either the Western or South-Eastern Hospitals, where post-scarlatinal diphtheria occurred to the extent of 3.6 and 2.5 per cent. respectively. But in 1892 a change was witnessed. Eighteen cases appeared amongst the 967 treated, an incidence of 1.8 per cent.; but of these 18 only 4 died, a not very high fatality of 22.2 per cent.

As bearing on the difference between 1891 and 1892 in the incidence of post-scarlatinal diphtheria at the South-Western Hospital, it may be mentioned that 420 cases of diphtheria were admitted in 1892, as compared with 211 in 1891; and that the average number of diphtheria cases remaining in the South-Western Hospital on the last day

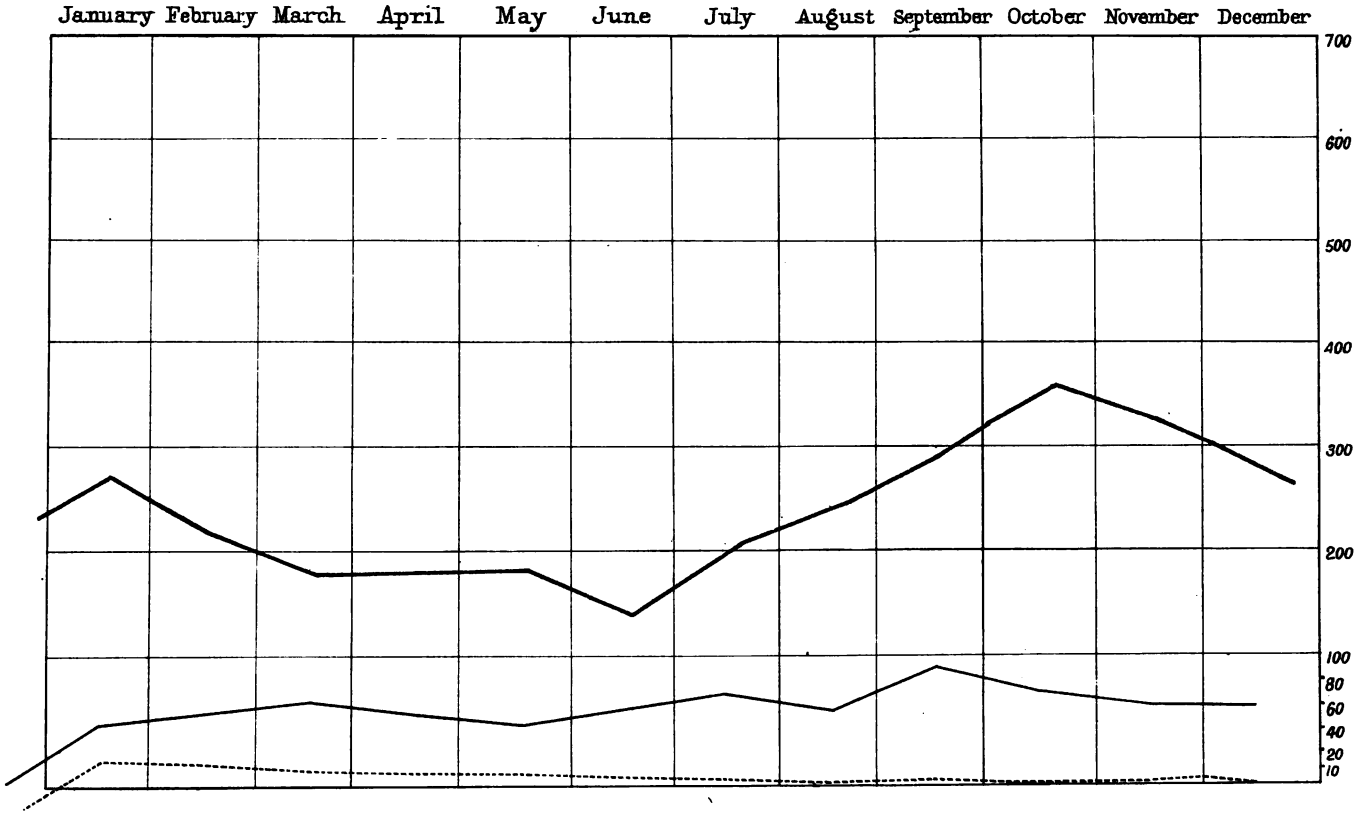
1890. (WESTERN, SOUTH-EASTERN AND NORTH-WESTERN HOSPITALS)

CURVE OF MONTHLY ADMISSIONS OF SCARLET FEVER (RED) & OF DIPHTHERIA (BLACK): WITH THAT OF THE MONTHLY INCIDENCE OF POST-SCARLATINAL DIPHTHERIA (DOTTED LINE).



1891. (WESTERN, SOUTH-EASTERN AND NORTH-WESTERN HOSPITALS)

CURVE OF MONTHLY ADMISSIONS OF SCARLET FEVER (RED) & OF DIPHTHERIA (BLACK): WITH THAT OF THE MONTHLY INCIDENCE OF POST SCARLATINAL DIPHTHERIA. (DOTTED LINE)



in each week was, in 1892, 44.9, whereas the average in 1891 was 21.2, or less than half. It may be, therefore, that greater aggregation of diphtheria cases in 1892 was associated with some intensification and exalted potency for spread in the virus of that disease. This is supported to some extent by the fact that although 5 scarlet-fever wards were implicated, 7 occurred in one ward, 4 in another, and 3 in yet another (or 14 of the 18 in 3 wards), under such circumstances of date of attack that in all probability 9 were due to personal infection in the wards.

I now present Table C, which shows the incidence of post-scarlatinal diphtheria on 14,136 completed cases of scarlet fever at the Northern Convalescent Hospital since its opening, *i.e.*, 1887-92.

TABLE C.—*Showing the Incidence of Post-scarlatinal Diphtheria on completed cases of Scarlet Fever at the Northern Convalescent Hospital since its opening* (1887-1892).

Year.	Scarlet Fever.	Post-Scarlatinal Diphtheria	Deaths from Latter.	Incidence per cent.	Case-Mortality.
1887 ...	1097	11	7	1.00	63.6
1888 ...	2752	31	14	1.1	45.1
1889 ...	1337	20	9	1.4	45.0
1890 ...	2829	38	24	1.3	63.1
1891 ...	1800	11	5	0.6	45.4
1892 ...	4321	46	31	1.06	67.4
1887 to 1892	14,136	157	69	1.03	44.5

N.B.—This Hospital, opened on September 25th, 1887, was temporarily closed from March 23rd to September 2nd, 1889. It did not receive diphtheria convalescents from the "acute" hospitals until October 26th, 1889.

The incidence has been pretty uniform throughout the six years, averaging about one per cent., and does not seem to have been appreciably affected by the reception of diphtheria-convalescents at the end of 1889. The lowest incidence occurred in 1891; this was never much above the average in any year. The lowest fatality occurred in 1889; the highest in 1892.

I will now proceed to analyse the occurrences of post-scarlatinal diphtheria at the Northern Hospital during

1888-92 in the same way as I have done those at the "acute" hospitals. No details exist for 1887.

1888.

Thirty-one cases amongst 2,752, or 1.1 per cent.; 14 fatal, or 45.1 per cent. In *time*, they thus occurred: January 2, March 4, April 4, May 2, July 4, August 2, October 5, November 5, December 7. *Time after admission* at the "acute" hospital was in all cases over four weeks; *after transfer*, 6 within one week; 14 between one and four weeks; 15 over four weeks. *Age:* $\frac{10}{31}$ of the cases and $\frac{5}{14}$ of the deaths under 5 years. *Wards:* eleven attacked; two of them had multiple cases due to personal infection.

1889.

Twenty cases amongst 1,337, or 1.4 per cent.; 9 fatal, or 45 per cent. In *time*, they thus occurred: January 7,* February 2, September 2, October 2, November 4, December 3. *Time after admission* at the "acute" hospital, all over four weeks: *after transfer*, one within a week; 11 from one to four weeks; 8 over 4 weeks. *Age:* $\frac{6}{20}$ of the cases and $\frac{5}{9}$ of the deaths under 5 years. *Wards:* eight attacked; inter-infection in one ward. Paralysis was noted in two cases; and in one case death ensued after 36 hours.

1890.

Thirty-eight cases amongst 2,829, or 1.3 per cent.; 24 fatal, or 63.1 per cent. In *time*, they thus occurred: January 8, February 4, March 1, April 3, May 3, June 3, July 4, August 3, September 2, October 6, December 1. *Time after admission*, all over four weeks; *after transfer*, three within one week; 16 from one week to four; 19 over four weeks. *Age:* $\frac{14}{38}$ of the cases and $\frac{14}{24}$ of the deaths under 5 years. *Wards:* 13 attacked; 6 cases due to inter-infection in them.

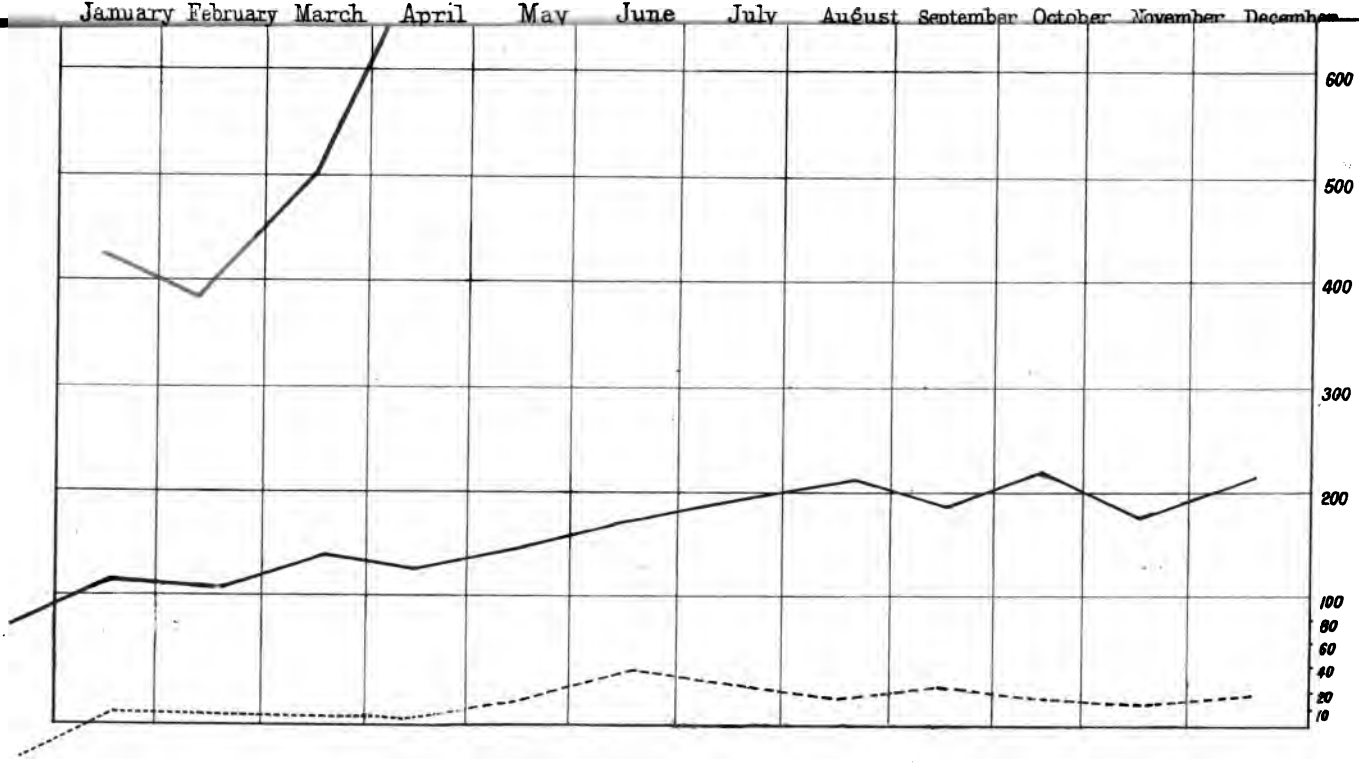
1891.

Eleven cases out of 1,800, or 0.6 per cent.; 5 fatal, or 45.4 per cent. In *time:* January 1, March 1, April 1, June 1, July 1, August 2, September 1, December 3. *Time after admission*, all over four weeks: *after transfer*, two within a week; five between one week and four; and four over four weeks. *Age:* $\frac{6}{11}$ of the cases and $\frac{4}{5}$ of the

* Including four attacked at the end of 1888, and included in the 1889 Report.

1892. (EASTERN, WESTERN, SOUTH-EASTERN SOUTH WESTERN AND NORTH-WESTERN HOSPITALS)

CURVE OF MONTHLY ADMISSIONS OF SCARLET FEVER (RED) & OF DIPHTHERIA (BLACK): WITH THAT OF THE MONTHLY INCIDENCE OF POST-SCARLATINAL DIPHTHERIA (DOTTED LINE).



deaths under 5 years. *Wards:* six attacked; no excessive ward-incidence or infection.

1892.

Forty-six cases amongst 4,321, or 1.06 per cent.; 31 fatal, or 67.4 per cent. In *time:* January 2, February 3, March 1, April 4, May 4, June 8, July 2, August 5, September 4, October 4, November 5, December 4. *Time after admission,* 11 from one to four weeks; 35 over 4 weeks. *Time after transfer,* 11 under one week; 23 from one to four weeks; 12 over four weeks. *Age:* $\frac{16}{46}$ of the cases and $\frac{15}{31}$ of the deaths under 5 years. *Wards:* 16 attacked; two wards had excessive incidence. Six cases due to ward-inter-infection.

SUMMARY OF NORTHERN (CONVALESCENT) HOSPITAL (1888-92).

$\frac{135}{146}$, or 92.4 per cent. of the cases occurred more than four weeks after admission at the "acute" hospital from which transferred.

$\frac{65}{146}$, or 44.5 per cent., occurred more than four weeks after transfer to the Northern Hospital.

47.2 per cent. occurred between one and four weeks.

8.3 per cent. occurred within a week, and therefore probably obtained their infection at the "acute" hospital.

As regards *season of year,* the quarterly incidence per cent. during 1888 and 1890 to 1892, when this Hospital was in full operation, was as follows:—

1*st quarter,*	27	amongst	2025	admitted,	or 1.3 per cent.
2*nd*	„	33	„	2796	„	or 1.1 per cent.
3*rd*	„	30	„	3231	„	or 0.9 per cent.
4*th*	„	36	„	3543	„	or 1.0 per cent.

This almost identical incidence in each quarter excludes the influence of season.

Age: $\frac{52}{157}$, or 33.1 per cent. of the cases, and $\frac{43}{69}$, or 62.3 per cent. of the deaths, were under five years; so that the concurrence of disproportionate incidence and fatality from 0-5 years is not observed as in the case of the "acute" hospitals, only a disproportionate fatality being noticed at that age.

I may here mention, as a supplement to the facts as to the Northern Hospital, that similar occurrence of post-scarlatinal diphtheria has taken place at the Gore Farm Convalescent Hospital recently opened. From July 3rd

to December 31st, 1892, 71 cases have occurred amongst 2,867 cases of scarlet fever admitted, an incidence of 2.1 per cent. on admissions. No diphtheria convalescents have been received here at all.

ADMINISTRATION.

As regards *nursing* administration, much diversity obtains at the Asylums Board hospitals. All are in agreement in having a separate nursing and ward staff for diphtheria; but considerable diversity exists with regard to the degree of separation of the hospital staff. This varies from complete separation from the scarlet-fever staff as at the South-Western Hospital, where two hospitals exist, and one is used almost entirely for diphtheria (the exception being a single scarlet-fever ward used chiefly for convalescents), to separation for ward purposes only; scarlet-fever and diphtheria nurses mingling at meals and in the recreation and bedrooms. At the Western Hospital no nurses from the scarlet-fever wards do ambulance duty in fetching patients from the homes to the hospital. With respect to *medical* administration, no factor is common, except that necessarily the Medical Superintendent and matron visit both scarlet-fever and diphtheria wards. At two hospitals, one assistant medical officer is distinct, and does no other wards; but at the others, the assistant medical officers visit scarlet-fever, diphtheria, and enteric wards indifferently. At some of the hospitals the assistant medical officer doing the diphtheria wards takes them first, at others last, at the remainder without any particular order. It is needless to say that the diphtheria patients are kept at each hospital quite distinct from the scarlet-fever patients.

With all the above differences, post-scarlatinal diphtheria has prevailed in similar fashion (though not to the same degree) at each of the hospitals. There is evidently no common factor of administrative shortcoming. Whether the hitherto small amount of post-scarlatinal diphtheria at the South-Western Hospital is to be associated with the greater rigidity of separation of the nursing and medical staff there, is a difficult point to determine. But the association is worth noting, with a view to the important suggestion (which might be made) of a totally distinct administration for diphtheria. I am not aware if this has been yet tried in this country. If it were, it would settle the etiological point as to whether post-scarlatinal diphtheria is

due at "acute" hospitals to mediate infection by an imperfectly separated staff.*

DRAINAGE.

Inasmuch as diphtheria is being constantly associated with drainage conditions—a much overstated view, as it appears to me—it may be as well to consider this point in connection with post-scarlatinal diphtheria at the Metropolitan Asylums Board hospitals. It may be said at once that all stages and varieties of drainage exist at these hospitals, from the old-fashioned system of twenty to thirty years ago, to the modern elaborate system of to-day. Post-scarlatinal diphtheria has prevailed in like degree in hospitals with ventilated, and in those with unventilated, soil-pipes; in hospitals with automatic flushing apparatus, and in hospitals without such appliances; in hospitals with elaborate systems of ventilation and disconnection, and in hospitals where these are of the most meagre and incomplete kind. In fact, the diversity is so great that no common factor of drainage defect can be pointed to as explaining the long-continued yearly recurrence of this condition of post-scarlatinal diphtheria. Then, again, as to the relative positions of the diphtheria and scarlet-fever wards with regard to the outfall of the hospital drainage into the main sewerage system. At some hospitals the diphtheria wards are nearest this outfall, at others farthest off. In the former case I could learn of no regurgitation of diphtheria-laden sewer-gas to the scarlet-fever wards above it; and in the more modern systems the disconnection of the ward drain from the main drain of the hospital is stated to be complete and satisfactory. I can certainly bear testimony to the efficiency of this disconnection at the Western Hospital. Further, in some hospitals—*e.g.*, Eastern—where the diphtheria wards are nearest the outfall, enteric wards above them, in exactly analogous position to scarlet-fever wards, have escaped diphtheria. *A priori*, knowing what we do of enteric, we would expect some invasion of these by diphtheria, if such defects existed. If additional evidence were wanted to show how inadequate to explain the facts a drain hypothesis is, it would be in the case of the North-Western and Western Hospitals, where cases of post-scarlatinal diphtheria have appeared in scarlet-fever wards and huts on a distinct and separate line of drainage from the

* It is, indeed, theoretically impossible to eliminate administration until this complete separation is made trial of.

general system of the hospital to which the other scarlet-fever wards or huts and the diphtheria wards belong.

This question of drainage has greatly exercised the Northern Hospital authorities, and various temporary expedients have been tried with respect to improvement of drainage, with but scant result in diminishing the incidence of post-scarlatinal diphtheria. I understand, however, that the whole drainage of this hospital has been recently renovated, and better means of ventilating and flushing have been provided. It remains to be seen if this will have any effect in checking the fatal post-scarlatinal diphtheria which has prevailed there ever since the hospital has been opened.

Warming.

The matter of warming deserves to be mentioned. Undoubtedly, there has been distinct under-warming of scarlet-fever wards at several hospitals of the Board, and this matter has received, and still is, I believe, receiving attention. But I cannot learn that such under-warmed hospitals have exhibited greater incidence of post-scarlatinal diphtheria than others better warmed. And further, in some of them in which this defect has been remedied, and the warming arrangements ameliorated, there has been no cessation or diminution of post-scarlatinal diphtheria. I am inclined, therefore, to dismiss this factor as an active or exciting agent in the etiology of post-scarlatinal diphtheria; though, of course, it is theoretically possible that lessened warmth may act as a predisposing cause of the malady, by inducing a catarrhal condition of the mucous membranes affected by post-scarlatinal diphtheria.

Conclusion.

To summarise the facts which I have presented to you, I have shown that post-scarlatinal diphtheria has occurred year after year at most of the hospitals of the Metropolitan Asylums Board during the nine years 1884-92.

That there has been a marked increase of the complication at the "acute" hospitals since diphtheria was received, although it had undoubtedly existed to a minor extent at some of them before diphtheria was admitted.

That at the Northern Convalescent Hospital it has existed both before and after the reception of diphtheria convalescents, and that its prevalence has apparently been inappreciably affeeted thereby.

That its age-distribution and fatality, as well as the time-curves of its incidence, seem to point to its greater *rapprochement* to diphtheria than to scarlet fever at the "acute" hospitals, though this is not so well marked in the case of the Convalescent Hospital.

That comparatively very few of the cases can be explained by outside infection or concurrent incubation, or by personal infection from case to case in the wards.

That no local ward conditions can be pointed to as responsible for the phenomenon.

That drainage defects fail to explain it, or deficiency of warming, except in the latter case in a subsidiary manner.

That administrative shortcoming is not altogether an efficient explanation, although in strict theory this cannot be altogether excluded, except at the Northern Hospital, where post-scarlatinal diphtheria existed to like extent before diphtheria was received as afterwards.

That there is some suggestion that the aggregation of acute cases of scarlet fever, or of diphtheria, or of both at the same time, caused by the system of drafting convalescents away, may have something to do at the "acute" hospitals with fostering the post-scarlatinal diphtheria which we have been investigating. It may be that the viruses of scarlet fever and of diphtheria, singly or conjointly, acquire by this aggregation an altered quality or an increased potency, which causes them to become, respectively, more readily transmutable and more easily diffusible.

And this leads me, in conclusion, to lay a few more or less pertinent questions before the Society.

First. Is post-scarlatinal diphtheria something inherent, intrinsic, and essential to scarlet fever? Or is it something accidental, extrinsic, and adventitious? And, if the latter, is the accident, in logical parlance, *separable* or *inseparable?*

Secondly. Is post-scarlatinal diphtheria a new and more determinate expression of the close affinity already known to exist between scarlet fever and diphtheria, whose specificities thus merge into one another, with but feeble line of cleavage?

Thirdly. If so, what is the environment under which such transmutation of specificity is accomplished?

And, lastly, how, seeing the high fatality as well as the inconvenience, administrative and social, attending the condition, may that environment, when determined, be

either abrogated, altered, or modified, so as to prevent the recurrence of post-scarlatinal diphtheria.

These and other questions arising out of this important subject, the fringe only of which I have touched this evening, I am content to leave to the members of this Society and to future inquirers.

ON AFRICAN HÆMOGLOBINURIC FEVER.

By PATRICK MANSON, M.D., M.R.C.P., LL.D.

(*Read: 15th March* 1893.)

Mr. President,—During the last ten or fifteen years our ideas on the subject of the fevers of tropical climates have been gradually undergoing a change. Venerable fancies, which generation after generation of writers had faithfully copied from their predecessors, have at last been challenged, and many of them abandoned for good. In this matter, as in so many others, we have ceased to reverence authority unless backed by demonstrable and demonstrated fact. We no longer believe that because Lancisi, or anyone else, said so and so, it must be so and so. Not many years ago malaria was held to explain every obscure problem in tropical pathology. There is a scientific ring about the word "malaria" which cloaked our ignorance in a respectable kind of way; there was something of comfort in it, too, like that which to the devout soul lay in the blessed word "Mesopotamia". In tropical practice it took the place which the word "gout" does in English practice. Merely to utter it and to prescribe calomel and quinine explained everything, and satisfied both patient and physician. It suffices no longer however. Tropical pathology and therapeutics have advanced with the advance of pathology and therapeutics in other departments of medical science. Reverence for authority and medical shibboleths has given place to reverence for facts and to diligent search for them, and to scientific methods. Notable fruit of this is that we have been able in recent years to sift from the rubbish-heap called "malaria", on to which our ignorances had hitherto been thrown, many diseases which our predecessors were content to call malarial. We have separated from it such diseases as tropical typhoid, relapsing fever, elephantoid fever, Mediterranean fever, anchylostomiasis, beri-beri, dysentery, liver abscess, and other though less important diseases. Within the last few years our views about these have undergone a very great change. But although the change has been great, I question if it has even yet gone far

enough. I believe that we are still in the trammels of tradition in many ways, that there are important diseases which we are still content to throw on the "malaria" rubbish-heap, but which, could we but get at the facts, we would see have little or nothing to do with malaria, but are specifically distinct and independent. I believe there are fevers and certain other pathological conditions which are still looked on as malarial, and that solely for no better reason than that they occur in tropical climates and in individuals who may previously have had attacks of genuine malarial fever. But because a man is living in the tropics, in a malarious district, and has had malarial fever, it is poor logic to conclude from this alone that the broken leg we are called on to treat him for is also malarial. It is equally illogical to conclude that because a man is living in the tropics, in a malarious district, and has suffered from malarial fever, that the particular fever or other disease we are called on to treat him for, is also malarial. Yet this is the kind of logic which is but too often applied to the diagnosis of tropical diseases, more especially tropical fevers. Practically it amounts to this;—because a fever occurs in the tropics it must be malarial. The medical mind cannot apparently disabuse itself of the "malaria" fetish. As so often happens in medical reasoning, coincidences are interpreted as existing in the relationship of cause and effect.

Just as there are many more human beings in the tropics and subtropics than in the temperate zones, there is a presumption that there are also many more diseases there, although we may not as yet have learned to recognise them. Therefore, if the pyretology of Europe includes some five or six fevers, it is not improbable that the pyretology of the tropics includes as many, if not more. And yet we credit the tropics with only three—yellow fever, dengue, and malarial fever. The two former are well defined; not so the last. It is true that certain fevers may be justly relegated to it, but I hold that there is a vast residuum of febrile disease credited to malaria, and usually called malarial, which has nothing whatever to do with malaria. I have seen many such cases. I call them "unclassed fevers". It has often occurred to me that writers of text-books, and especially systematic writers on tropical disease, would do well to imitate the old cartographers, who, when they came to lay out the map of Africa, wrote across much of it "unexplored territory".

I propose to say something about one of these doubtfully

malarial diseases, viz., blackwater fever, or, as it is sometimes called, hæmaturic fever, or, better, hæmoglobinuric fever; a disease hitherto classed as malarial, but which I think has been so classed on insufficient grounds. I do not say that it is not malarial; but I do say that it has not been proved to be such, and that there are strong reasons for thinking that it is a disease *sui generis*, one of the "unclassed" fevers I have referred to; and in the following remarks I hope to bring forward adequate reasons for at least suspense of judgment in the matter.

Before proceeding it might be well if I state what I mean by "malaria" and "malarial disease". I disregard the etymology of the word altogether. *Mal aria* means simply bad or vitiated air. But when we speak of "malaria" we mean something of a much more definite nature than the etymology of the word would indicate; we mean something specific in the shape of a special air-borne germ or poison; and when we speak of malarial disease we mean a certain specific type of disease, produced by this specific air-borne germ or poison. It would be easy to say that malaria is the *plasmodium malariæ*, or Laveran's bodies, and that malarial disease is an outcome of the action of these on the human body. This may be a perfectly correct definition, and in time it may prove to be such; but as yet it is premature. As yet we can only define malaria by its effects. I would say, then, that malaria is that poison, or those poisons or germs which give rise to the intermittent fevers—quotidian, tertian, and quartan ague—and the remittent fevers which seem to spring out of or merge into these; which at the same time gives rise to forms of hypertrophy of the spleen, and to the deposit of a peculiar kind of pigment in certain organs—notably the spleen, bone-marrow, liver, and brain; and, further, that its effects are to a very great extent counteracted by quinine. With the exception, perhaps, of pigmentation, none of these things is in itself peculiar to malaria; but taken together they are sufficiently characteristic for us to recognise it by.

Unfortunately, owing to the paucity of well-made and well-recorded *post mortem* examinations, we are not in a position to apply the pigmentation test in the case of hæmoglobinuric fever. We are therefore obliged to fall back on the clinical and therapeutical tests. The verdict they give is at best very doubtful; and this doubt is further accentuated by certain epidemiological facts in the history and geographical distribution of this disease to which I propose specially to direct your attention.

Before proceeding in this, as it is of importance that the disease of which I am to speak should be distinctly defined, I shall try, as briefly as I can, to give a sketch of its leading clinical features. This I would not inflict upon you could I refer you to a good description by any of our standard English medical writers. And here I would remark, in parenthesis, that it is a singular thing that of our numerous systematic writers on tropical disease, not one of them describes hæmoglobinuric fever, although it is one of the commonest diseases among Europeans in Africa, as well as one of the most deadly. There is no excuse for this neglect by our writers, for there are good descriptions of it by English observers; but these our standard authorities have ignored, as they have also the extensive and most valuable French literature on the subject. Among English writers I might refer to Easmon, Eyles, Sullivan, Prout, and especially to the excellent monograph on the fevers of the Niger by Crosse. Among French writers I would specially refer to Dutrouleau, Bérenger-Féraud, Nielly, Leroy de Méricourt, Corre, Roux, Kelsch and Kiener, and many others; indeed, it is to French writers that we are indebted for the best as well as for the earliest accounts of this important disease.

On the evening of 26th March last year I saw a gentleman in London who had just returned from travelling on the Congo. He was thirty years of age. I knew him a year before as a very active man of sound constitution, and a total abstainer. Soon after his arrival out on the Congo, and off and on all through the nine months he spent there, he had attacks of fever. Only one of them was associated with hæmoglobinuria and of especial gravity. The others, though trying, were not of sufficient importance seriously to interfere with his work, or his moving about the country and penetrating far into the interior of Africa. He left the Congo on the 15th of February in company with a lady, his cousin, who had lived in Africa for three years, and who had just lost her husband there from hæmoglobinuric fever. On the voyage to England my patient enjoyed fair health, though he had a couple of slight fevers *en route*. He was in good health when he landed at Plymouth on the 27th March. He did not remain many hours there, but took the first train to London. The weather was unusually cold and bleak at the time. The next day he was feverish more or less all day, and at 5 P.M. he had a smart rigor, quickly followed by high fever. He took at once a dose of calomel and

quinine, and went to bed. On using the chamber-pot, he noticed that his urine was of the colour of port wine. I saw him five hours later, about 10 P.M. He was then in bed, his skin hot and perspiring freely, his pulse quick, temperature 104.2°; he had some headache, and was inclined to toss about a little; he had also lumbarache and general feverish distress, and his skin was yellow as a guinea. Next day when I saw him in the afternoon the fever had abated, and the urine, although still discoloured, was less dark. On the third day the patient was practically convalescent, although weak, anæmic, and yellow skinned. He gradually improved, and is now fairly well, although there was a slight break-down last autumn from overwork.

Strange to say, a day or two after this patient began to mend, his cousin, the lady who had travelled home with him, was seized in exactly the same way, the disease running pretty much the same course. Her temperature was higher, and for a short time stood at 107°. Like the other patient, she had been feverish all day before definite rigor set in, and with the rigor the urine became dark. I believe this was her sixth attack of hæmoglobinuric fever.

As I have said, I saw the gentleman about five hours after the initial rigor. His temperature was then 104.2°; he was sweating freely; he was passing from time to time urine of a port-wine colour; and his skin was deeply stained. As the urine passed showed no sign of clearing it was evident that a process of blood-destruction was actively proceeding. I pricked his finger and placed some of his blood under the microscope. It was at once apparent that I was contemplating a ruin, an army, so to speak, in stress of battle, the regiments broken and scattered, the soldiers many of them wounded or dead. I noticed first that the rouleaux arrangement of the corpuscles was exceedingly imperfect, hardly existed, in fact, the corpuscles lying together in clusters, or floating about singly. I noticed also that the individual corpuscles varied between very wide limits in size, shape, and depth of colour. Many of them exhibited a marked disposition to buckle up, cup, or fold on themselves, as if from limpness and imperfect filling of the cell-wall. Some were absolutely colourless, just visible in the liquor sanguinis, but utterly devoid of colouring matter; others were full-coloured, and between these extremes there were discs with every grade of coloration. There were noticeable, also, numbers of microcytes, both full-coloured or pale, or almost colourless, and

varying in diameter from about the 1-10,000th of an inch up to the size of an ordinary blood-corpuscle. Some of the corpuscles were "tailed", and when two would part company the tendency to stick together and tail out at the point of contact was very marked.

I examined the patient's blood again on the following afternoon. The urine had now become much clearer, and the body temperature had fallen, and the blood, too, had become more natural in appearance. Rouleaux formation was more perfect, microcytes were fewer in number, and there was greater uniformity in the size and shape of the red discs, and less tendency to buckle up and to tail. Along with this improved appearance of the red corpuscles there was a very manifest increase in the number of white corpuscles.

The urine passed during the first hours of the attack, when seen in bulk, appeared quite as dark as port wine; when in a thin layer, or when diluted, it was of a reddish brown colour. On standing, a copious light brown sediment formed, which, under the microscope, was found to be made up of a variety of elements:—1st. Innumerable straight, very dark brown, large, granular casts, some short, others fairly long. 2nd. A large amount of a light brown granular material. 3rd. Small, unpigmented, oval or round, single or double nucleated epithelial cells. 4th. Oval bodies, single, in twos or threes, and in groups; about these I shall have more to say presently. 5th. Ragged pieces of black pigment. After decanting the supernatant fluid, and washing the sediment in two or three waters, I found that the latter was soluble for the most part both in nitric acid and in liquor potassæ. On adding cold water to the nitric acid solution a precipitate was thrown down which redissolved on the application of heat. Alcohol or chloroform did not dissolve the sediment. Applying liquor potassæ to a slide of the sediment, whilst viewed through the microscope, it was seen that the brown granular matter and the dark brown casts were rapidly dissolved, whilst the epithelial cells were rendered very clear; but there was no corresponding action on the particles of black pigment, or on the ovum-like bodies I have alluded to. On boiling a specimen of the urine of the 28th March, a coagulum of about one-third albumen formed, and, as it subsided in the test tube, carried down with it all the colouring matter dissolved in the urine, the upper layer of which was thus left a light straw colour, clear and transparent. The urine of the 29th behaved similarly, the deposit of albumen being

very much smaller—about a fifth or sixth only. This last urine was acid, and had a specific gravity of 1020. It was the colour of Malaga wine, and deposited a considerable sediment.

Such is a short account of a case of African hæmoglobinuric fever occurring in England.

In the countries in which this disease is endemic the ordinary forms of malarial fever are particularly rife; and it has been remarked also that the subjects of hæmoglobinuric fever have almost invariably suffered considerably from recurring attacks of fever assumed by them to be ordinary intermittent and remittent. As a consequence of these attacks, or simply of what is considered to be chronic malarial poisoning, such individuals—as, for example, the patient whose case I have just described—come to be in a more or less anæmic, cachectic condition. Once a week, or once a month, or perhaps not so often, such an individual has his day or two of fever which he treats with a purgative and quinine. The attacks are in themselves not severe, for in a day or two the patient can get about as usual and attend to his duties. But, after a year or so of this, a time comes when he has an attack which turns out to be one of perhaps exceptional severity and gravity. He has the accustomed preliminary febrile malaise leading up to rigor, pyrexia, and diaphoresis, with complete intermission, to be followed next day, or two days later, by a repetition of the same; or perhaps—and this is the most usual course—there may not be a complete intermission, but the fever assumes a remittent type of perhaps an irregular character. And it would seem that these irregular, ill-defined forms of fever are somewhat characteristic of the type of the disease tending to end in hæmoglobinuric fever. A gentleman, who not only had personal experience of the disease but had nursed members of his own family and many of his colleagues during their attacks, informed me that on the Congo old residents always regard a fever with a low maximum temperature and an imperfect intermission—say, for the one 102°, and for the other 99.5°—with a rise of a degree or half a degree daily, as much more serious and much more likely to be suddenly complicated with hæmoglobinuric symptoms than a frank intermittent with a high maximum temperature of 105° or 106°, but with complete apyrexia in the intermission. Be this as it may, on the second, third, or fourth day of what appears to be an obstinate or smart attack of one of his ordinary and familiar fevers—sometimes even on the first day,

sometimes again not until after a week of fever—the patient is seized with an unusually severe rigor, and generally, though not always, with severe bilious vomiting and headache. The attack progresses in the ordinary way with this exception, that when he passes water, sometimes during, or sometimes after, rarely before the initial rigor, he finds that his urine is very dark, and, should he look at himself in the glass, that his skin has rapidly become of a bright yellow colour. The urine becomes dark first, the skin yellow rather later; in either event the change in colour is rapidly brought about. Concurrently with the darkening of the urine the loins begin to ache excessively, and the liver and spleen may enlarge somewhat and be very tender on palpation. At first the urine is only slightly darker than normal, but it rapidly passes through shades of malaga colour, port-wine colour, to almost inky black; and as it becomes darker it becomes scantier, thicker, and, in severe cases, of a gummy consistence. Pyrexia succeeds the cold stage, bilious vomiting persists, and perhaps several loose bilious stools are passed; or, on the other hand, there may be constipation, or vomiting may be entirely absent. Meanwhile the fever progresses, and the hot stage sets in, to be followed in due time by a copious diaphoresis. With the establishment of this the more distressing symptoms gradually abate; the loins cease to ache, the liver and spleen become less tender, and the bilious vomiting, if present, gradually subsides. At the same time, in favourable cases, the urine becomes less dark in colour and more copious, passing through shades of dark brown, malaga, yellow, and, finally, becoming clear and limpid and often very copious. It may take a day or two, however, for the urine to clear completely, and even longer before the skin and sclera lose the yellow tint which they had so suddenly acquired. On the subsidence of the fever and the clearing of the urine the patient recovers for the time being, with the exception that he is left profoundly anæmic and weak as if he had had a severe hæmorrhage, and that he is henceforth very liable to a recurrence of hæmoglobinuric fever.

Such a description applies to a somewhat mild attack of the disease. Unfortunately, all do not terminate so favourably. A fatal issue is far from being uncommon, and appears to be brought about in one of the three following ways: First, the fever and the hæmoglobinuria may take on a continued or remitting type and bring about death by simple exhaustion; second, the fever and hæmo-

globinuria may cease after perhaps one or two relapses; yet though these finally cease the patient is left so weak that he may die after a few days of sheer anæmia and with symptoms such as follow a flooding. These two types are bad enough, but there is a third which is much worse and almost invariably fatal. In it death seems to be brought about by an uræmic condition, the result of plugging of the renal tubules by hæmoglobin or its derivatives, or of a consequent nephritis. There is the usual smart fever, the vomiting, and the dark urine; but instead of, as in favourable cases, the urine after a time becoming gradually lighter in colour and more copious, it becomes more scanty, of a thick, syrupy consistence, and finally completely suppressed. Recovery from this condition is quite exceptional. Death usually ensues after a few days—the secretion never becoming properly re-established, although there may be no recurrence of fever. In these cases the tongue becomes dry, the patient apathetic or delirious, and, finally, a convulsive seizure may end in coma and death.

If the dark urine characteristic of this disease is examined, it is found to deposit a copious sediment of a colour somewhat lighter than the blackish or brownish fluid in which it is suspended. Under the microscope this sediment is seen to consist of much dark brown, amorphous, granular matter; numerous tube-casts of a similar material embedded in a hyaline matrix; epithelium from different parts of the urinary tract; a few exudation corpuscles; and a very few—sometimes hardly any—red blood corpuscles. On boiling the urine a copious deposit of albumen, amounting to a half, or even more, sometimes not so much, is thrown down. If the chemical and spectroscopic tests for hæmoglobin are applied, the presence of this substance or of its derivatives is readily detected; and it is to these, and not to bile pigment, which is usually absent, that the dark colour of the urine is due. In fact, the physical characters of the urine are those of the hæmoglobinuria we are familiar enough with in this country.

If a slide of the patient's blood drawn during the acute stage of the fever and for a day or two thereafter is examined with the microscope, evidence of very active blood destruction is revealed. Rouleaux-formation hardly exists, and this is found to be combined with an extreme degree of poikilocytosis. The red corpuscles are much distorted, and vary not only in shape but also in size and in colour. Microcytes are abnormally abundant, much granular matter floats about in the liquor sanguinis, and in

every field absolutely colourless discs and rent and crenated corpuscles are to be found.

There are many other interesting points in the clinical tableau of hæmoglobinuric fever to which I have not alluded. In the foregoing brief description my object has been not so much to make a complete picture of the disease, but rather to call attention to its salient clinical features, so as to make plain what I mean by the term hæmoglobinuric fever. Nor do I propose to enter on a consideration of its pathology further than to say that hæmoglobinuric fever is regarded by most writers on the subject as being merely an extreme expression of ordinary malarial poisoning; the hæmoglobinuria being the result of an excessive and rapid development of that exaggerated hæmolysis which always accompanies, in greater or less degree, the malarial state, whether acute or chronic, and which, when moderate in amount, is generally believed to bring about, by a well-known physio-pathological process, the anæmia and policholia of malarial attacks. It is asserted that when this hæmolysis is very excessive, and is suddenly produced, and is in degree beyond the physiological powers of the liver to cope with, the liberated hæmoglobin is not all converted into bile pigment but floats about in the liquor sanguinis, or is deposited in the tissues until its excretion in a more or less unchanged condition can be overtaken by the kidneys. Hence the icteric tint of the skin, which is not produced by bile any more than is the dark colour of the urine, the colour in both instances being derived wholly from the hæmoglobin. There are theorists who even go a step further than this; they pretend to explain the exact mechanism by which the hæmoglobinuria is produced. They say—and in saying this they assume what, as far as I know, has not yet been proved, viz., the invariable presence in the blood in these cases of a prodigious swarm of Laveran's bodies,—they say that the plasmodia in the course of their evolution rupture the blood discs, and so liberate the contained hæmoglobin. I shall have something to say on this presently; meanwhile I would again point out that, with the majority of writers, hæmoglobinuric fever is only a severe form of ordinary malarial fever.

This brings me to the principal object of this paper, which is to suggest caution in adopting such an ætiology and pathology. The grounds on which I would base this caution are twofold—clinical and epidemiological. I shall not have much to say from the clinical standpoint; but,

before passing to the epidemiological side of the question, there are one or two points of a purely clinical character to which I would first briefly direct attention.

It is reasonable to think that high degrees of malarial poisoning are, unless in the algid type of pernicious fevers, accompanied by proportionate degrees of fever. Therefore, if we are to regard hæmoglobinuric fever as an expression of a high degree of malarial poisoning, we might expect that it would be accompanied by a corresponding amount of fever. But this is very far from being the case. Generally, of course, in hæmoglobinuric fever the fever is smart, sometimes amounting to hyperpyrexia; but not infrequently it is very slight or insignificant, and yet in such a case the associated hæmoglobinuria may be decided or even severe. Thus Corre narrates a case of a native woman at Nossi-be who refused to lie down during an attack of hæmoglobinuric fever; it is evident that in her case fever was absent or only trifling. Crosse, too, mentions a case in which during four attacks of hæmoglobinuria there were no marked constitutional symptoms or fever of importance. In conversing with several gentlemen, who had themselves suffered from the disease, I have been struck with the mild character of the constitutional symptoms they describe as accompanying some of their attacks.

Another clinical fact I may remark on is the abruptness with which the fever concludes, sometimes within a few hours, after the explosion of the hæmoglobinuria. Malarial fevers of severe type do not come to an end thus abruptly, and are not thus accompanied by low temperature and absence of constitutional symptoms.

Then, again, the peculiar cyclical character of the antecedent fevers which for months, or perhaps for years, precede the attack which is accompanied by hæmoglobinuria. These antecedent fevers seem, in some instances, to be very mild, and to recur with wonderful regularity once a month or once a fortnight, or at some more or less regular interval. This spacing of the cycle is not quite like that of an ordinary malarial fever, which is, as a general rule, either quotidian, tertian, or quartan.

The general employment of quinine in the treatment of hæmoglobinuric fever and of the recurring fevers which lead up to it—and which really seem to be hæmoglobinuric fever without the hæmoglobinuria, if I may so describe them—might be advanced as evidence for the malarial nature of the disease. But before concluding that this

popular employment of the drug is really founded on its curative powers and not simply on fashion, we ought to have some accurate knowledge of the natural evolution of the disease unmutilated by quinine. I have not come across the record of any such case; but we can see, if we refer to the published cases of hæmoglobinuric fever, that the fever has in many instances persisted for several days in spite of liberal dosing with quinine from the outset.

From a purely clinical stand-point I cannot see that there is sufficient evidence for regarding hæmoglobinuric fever as an ordinary malarial disease. Such evidence suggests rather, especially when taken along with the epidemiological facts I am about to detail, that in most instances we should regard the cases met with in practice as being of a compound character, resulting from two morbid influences: first, malaria proper; second, another poison, which determines a mild type of fever, but which also tends to produce hæmoglobinuria. But just as malaria may exist without this mild fever or its associated hæmoglobinuria, so hæmoglobinuric fever may exist without malarial complication. Clinical facts tend to show that the occurrence of the one type of disease favours the explosive manifestation of the other, and thus it is that so many of the cases appear to be of a dual character.

Looking at the question from an epidemiological point of view there are three things which particularly strike me:

First. Hæmoglobinuric fever, though not absolutely unknown in one or two places bordering on the Mediterranean, is practically confined to the tropical and subtropical regions of Africa and America. It is almost if not altogether unknown in India, the Eastern Peninsula, the islands of the Eastern Archipelago, North Australia, and China.

Second. Whereas hæmoglobinuric fever is by no means a rare occurrence in Europeans who have returned to Europe from the endemic area of the disease in Africa, there is no record of such an occurrence in malarials who have returned to Europe from the malarial countries of Asia and Australia.

Third. There is no distinct account of hæmoglobinuric fever in medical literature prior to 1850; and there is some evidence that of late years the endemic area of the disease has extended its borders.

Now, if any or all of these propositions can be established it is evident that we have in hæmoglobinuric fever

something different from ordinary malarial infection. For if hæmoglobinuric fever were only an expression of malaria why is it not frequently met with in India, China, and other highly malarious countries outside the African and American continents? Why, if it is a common expression of malaria in subjects returning from Africa, is it not at all events an occasional expression of malaria in malarials returning from other countries? And why is it that so striking a disease had not been described before 1850, and that it appears to be extending its area of late years, seeing that malaria has existed from time immemorial in many countries, and certainly in those in which hæmoglobinuric fever seems to have appeared but lately?

I shall examine several of these points in some detail.

First. With reference to the relative geographical areas of ordinary malaria and hæmoglobinuric fever.

In the tropical zone of Africa, especially on the western side of the continent, Blackwater fever, or Hæmaturic fever, as it is called there, is so common that every European frequenting these parts is familiar with it. In many districts nearly every European expects to get it sooner or later if he remains in the country long enough. There are reliable statistical data for this statement. The French writers have compiled valuable statistics on the subject, and these I am enabled, by the kindness of Dr. Grattan Guinness, to supplement by others of an interesting and convincing character.

According to Bérenger-Féraud 38 per cent. of Europeans residing at certain French settlements at Gaboon and on the Gold Coast, 28 per cent. of those residing on the Upper Senegal, about 15 per cent. of those at Cozamance and on the Rio Nunez, about 8 per cent. at Cayor, and from 1 to 3 per cent. of the European inhabitants of St. Louis and Gorée are annually attacked with hæmoglobinuric fever.

I have arranged in tabular form certain statistics showing the mortality among the *employés* of the Congo Free State from October, 1878, till the end of August, 1892. The figures deal with 938 Europeans. Including the time occupied on the voyages to and from Africa, the average duration of each man's service amounted to about 20.25 months. Of the 938 men, in the course of this very short service of considerably less than two years, 157, or nearly one-sixth, died. Of the 157 deaths, seventeen are attributed to hæmaturic fever. But as the returns of death were not very accurately made—as might be expected under the circumstances—we may be certain that while all those who

are stated to have died of hæmaturic fever did so die, it is highly probable that of the fifty-five deaths attributed to fever, and of the nine of whom the cause of death was not stated, not a few died of the disease we are considering. We are under the mark, therefore, when we conclude that 11 or 12 per cent. of the deaths of those Congo Free State *employés* were caused by hæmoglobinuric fever. Corre states that the mortality in this disease varies in different countries and at different seasons of the year, ranging from 11 per cent. to 50 per cent. of those attacked. Probably 25 per cent. may be taken as an average mortality. Applying this to the Congo State statistics, it would give us about seventy-eight cases of hæmoglobinuric fever in the total number of 938 men during the twenty months of their residence in Africa. This, however, does not represent quite faithfully the true position of the morbidity and mortality and risk to European life from the disease. Ordinary remittents and intermittents and other climatic diseases like dysentery, sunstroke, and tropical typhoid, are much more prone to attack the new-comer than the old resident. But the case is exactly the opposite with hæmoglobinuric fever. It may and does attack the new-comer, but in the majority of instances it is the disease of the acclimatised—of the old resident. Thus, of the fifty-five deaths from "fever" mentioned in the Congo State statistics the average duration of residence in Africa of the victims was only twelve months; whereas in the case of those who died of hæmoglobinuric fever it was 31.8 months. So that if the average duration of residence of the *employés* of the Congo Free State had been five years, instead of something less than two, the proportion of deaths from hæmoglobinuric fever would have been very much greater. Of the seventeen deaths actually registered as being from hæmoglobinuric fever, only two of them occurred under nine months' residence; the majority had been in the country over twenty months.

TABLE *showing the Mortality, the Causes of Death, and the Duration of Residence on the Congo of those who died of* 938 *employés of the Congo Free State with an average age of* 29 *years and an average residence there of* 20.25 *months. The statistics apply to the period between October,* 1878, *and August* 30*th,* 1892.

Disease.		Deaths.		Length of Residence.	
Fevers	Fever	42	55	$12\frac{2}{7}$	12 months.
	Bilious fever	6		$14\frac{1}{6}$	
	Brain fever	6		$6\frac{1}{3}$	
	Intermittent fever	1		4	
Hæmaturic fever			17	$31\frac{14}{17}$	„
Intestinal flux	Dysentery	14	17	9	$11\frac{8}{17}$ „
	Intestinal dyspepsia	1		28	
	Bowel complaint	1		13	
	Chronic diarrhœa	1		28	
Hepatic	Liver complaint	3	5	$16\frac{1}{3}$	$15\frac{4}{5}$
	Liver abscess	2		15	
Sunstroke			8	10	„
Nervous system	Brain disorder	1	5	1	$12\frac{2}{5}$ „
	Apoplexy	2		15	
	Delirium tremens	1		24	
	Meningitis	1		7	
Pulmonary	Pneumonia	1	2		$2\frac{1}{2}$ „
	Congestion of the lungs	1			
Miscellaneous	Diabetes	2	6	5	$9\frac{1}{3}$ „
	Anæmia	1		16	
	Heart disease	1		3	
	Blood poisoning	1		14	
	Congestion	1		13	
Violent deaths	Drowning	11	26		14 „
	Other accidents	2			
	Killed in fight	4			
	Suicide	4			
	Killed by buffalo	1			
	„ hippopotamus	2			
	„ crocodile	1			
	„ snake	1			
Fatigue and exhaustion			7	14	„
Not stated			9	$14\frac{3}{9}$	„
			157		

The statistics of several of the missionary societies on the Congo, with which Dr. Grattan Guinness and others have very kindly supplied me, tell, as far as they go, exactly the same story. Thus, of 161 missionaries who have lived in this region in recent years 43 have died in the country. The figures are as follows:—

	Numbers.	Invalided.	Died.
Congo Balolo Mission	26	... ...	2
Baptist Missionary Society	60	... 3 ...	23
Livingstone Inland Mission	44	... 4 ...	11
Swedish Missionary Society	31	... .	7
	161	7	43

The returns as to the exact cause of death are complete

only as regards the Baptist Missionary Society. Of the 23 deaths in this mission six are attributed to hæmoglobinuric fever.

As regards other parts of the West Coast of Africa, we have the evidence of Easmon (*Med. Times and Gaz.*, Aug. 29th, 1885; and a special report made for the Government of the Gold Coast) and Prout (*Lancet*, 1st Aug., 1891) as to the frequency of the disease on the Gold Coast; of Crosse who in his recent work already referred to, on the *Malarial Fevers of the River Niger*, gives similar testimony as to that district; and of several of the Army Medical Reports in which allusion is made to the disease as it affects Sierra Leone, Cape Coast Castle, and other British settlements in that part of the world. There cannot, therefore, be the slightest doubt about the extreme frequency of hæmoglobinuric fever all along the western side of tropical Africa.

On the Eastern side of the continent it may not be quite so common, but still it is now well known to be far from rare in many districts. Thus it is well known and has often been described by the French naval medical officers stationed at Nossi-bé, Mayotte, and Madagascar. Dr. Castle (*Lancet*, 25th April, 1891) gives a short description of what undoubtedly is hæmoglobinuric fever at Usambara, East Central Africa. Our naval medical officers have frequently met with it on the Zambesi; and Dr. W. A. Scott (*Edin. Med. Journ.*, Nov., 1892) gives an admirable and unmistakable description of two cases occurring in the Shiré highlands, British Central Africa. Surgeon-Captain Parke describes his own attack of hæmoglobinuric fever when crossing the eastern part of the continent; and doubtless there are other allusions to this disease in periodicals which have escaped my notice. What I have said is, I trust, sufficient to establish the fact of the occurrence of the disease in many parts of tropical Africa, and its extreme prevalence in some.

As regards America there is abundance of evidence of the existence of hæmoglobinuric fever both in North and South America, and in the West India Islands. The medical journals of the Southern States of the Union record numerous cases of local origin. Sullivan speaks of its frequency in Cuba. Many French writers testify to its prevalence in Martinique and other French possessions in the West Indies and in South America. Prof. Magalhães of Rio de Janeiro informs me that he has not met with the disease in Brazil; but further north, in Venezuela, it is well known, and Dr. Ackers of Caracas tells me that,

though not common in the highlands of that country, it is exceedingly prevalent in the plains and very deadly there.

The case is very different as regards Asia. By diligent search in such Anglo-Indian literature as seemed likely to yield the information I have done my best to procure reliable evidence for the existence of hæmoglobinuric fever in India; but I have completely failed to get anything like a description of cases at all corresponding to the African or American disease. Dr. Norman Chevers (*The Diseases of India*, 1886), a man of great erudition and experience, and also a keen and enthusiastic observer, makes no mention whatever of such a disease. He mentions the frequency of the various forms of hæmorrhage to which the victims of malaria are subject, and he shows that he was familiar with the literature of ordinary hæmoglobinuria—so that he was not likely to fail to observe and note so remarkable a disease as hæmoglobinuric fever had he encountered it—yet, in his elaborate work, he makes no allusion whatever to such a condition. Maclean (*Reynolds's System of Medicine*), Fayrer (*Climate and Fevers of India*, 1882), and Martin (*The Influence of Tropical Climates*, 1853) are equally silent on the subject. Morehead (*Researches on Disease in India*, 1860) makes no specific mention of hæmaturia or hæmoglobinuria in fever. He refers to jaundice as occurring in remittent fever, and he does mention one case in which the urine was of a deep brown colour, but he gives us no clue as to the cause of this colour, and we are left to infer that it arose from biliary staining, or possibly from ordinary hæmaturia. Morehead was a very close observer, and certainly would not have overlooked the occurrence of hæmoglobin in the urine had so striking an appearance been at all common in his field of observation. Moore (*Manual of Diseases of India*, 1882), speaking of the complications of fever, says: "The occurrence of jaundice during fevers has led to the term 'bilious remittent'. In this form of the malady jaundice often appears from the outset, and vomiting of dark-coloured matter is an early symptom. The urine is often coffee-coloured, owing not to bile, but to blood." But he does not state if this remark is founded on personal observation of what actually occurs in India, or if it is borrowed from others and possibly applicable only to disease in some other part of the world. And again, speaking of intermittent fever, he says, "albumen, renal casts, and blood will probably indicate some pre-existing tendency to kidney-disease". All this is some-

what indefinite, and may not refer to India. I do not think that either Morehead or Moore could have seen, or that they refer to genuine hæmoglobinuric fever. Hirsch cites Day (*Indian Ann. of Med. Sc.*, 1859) as authority for the existence of the disease in India; but, on turning to the article referred to, I find that what Day describes is simply "bilious remittent", and that there is no reference whatever in his article to anything which could be construed as hæmaturia or hæmoglobinuria.

The only allusions to a condition at all resembling African hæmoglobinuric fever which I can find in recent Indian medical literature are by Firth and Notter (both in the Appendix to the *Report for* 1885, *Army Med. Dep.*, pp. 367-377). The former, in 1,033 cases of intermittent fever, found that 25 were accompanied by jaundice simply—that is, 2.5 per cent.; none had icteric urine, and only 11 had hæmatinuria, or about 1 per cent.; but he does not say anything about the amount of hæmatin in these cases, and, from the context, we are led to infer it was merely a trace. Of 221 cases of remittent fever 4 had well-marked jaundice alone; 2 had jaundice together with hæmatinuria; and 2 had jaundice, hæmatinuria, and icteric urine. Two of the cases came under his own observation—one at Mian Mir, the other at Amritsar. The former had well-marked jaundice, and, on the day following the appearance of the jaundice, the urine became dark smoke-coloured and gave a biliary reaction. It contained hæmoglobin, a few blood-corpuscles, but, until two days before death, no albumen. The second case appears to have been similar, with the exception that the urine "was at no time albuminous". Notter says: "A form of malarial disease which I have seen in Meerut, and in no other station, is paroxysmal, congestive hepatic hæmaturia. The hæmaturia intermits—one day clear and without albumen, the next day chocolate-brown and containing much albumen, the *débris* of blood-cells, casts, and coloured granules, but no corpuscles." It is difficult, from the very meagre account we have of these cases, to come to a definite conclusion about their nature. In Firth's cases the absence of albumen and the small amount of hæmoglobin—only sufficient to make the urine smoky—is unlike African hæmoglobinuria. In Notter's cases the colour of the urine and the presence of a large quantity of albumen conform more to the African disease; but the absence of albumen on alternate days seems to negative this idea, as in African hæmoglobinuric

fever the albumen persists for a day or two after the hæmoglobin has disappeared from the urine.

The older Indian writers, with the majority of their modern successors, are equally silent on this subject. The reason for their silence is evident; they concerned themselves only with Indian disease; they did not write of hæmoglobinuric fever in India because it did not and does not, in its typical form, exist there. Certain French writers say that our English authors have overlooked this condition and confound hæmoglobinuric fever with ordinary bilious remittent. But this is not so. English writers, when they have the chance of seeing the disease in Africa, as some of them in recent years have had, and as Sullivan had in Cuba, recognise it, and regard it as a distinct form of fever—quite distinct from bilious remittent. We must conclude, therefore, that hæmoglobinuric fever does not occur in India, or is exceedingly rare there. Either this, or we must—contrary to all experience in other medical matters—indict the profession in India as being extremely careless and singularly deficient in the faculty of observation, and as having for all these years entirely overlooked a most striking, obtrusive, and important medical fact. This, of course, is absurd.

As regards the other parts of the Far East, I can find no good grounds for believing that hæmoglobinuric fever exists there any more than in India. If it does exist, it is found in very limited districts only. I have interrogated, either personally or by letter, many of my professional friends in the Straits of Malacca and in China, but, with one or two exceptions, one and all agree in saying that they have never seen a case of the disease, and several of them absolutely deny the existence of hæmoglobinuric fever in the districts with which they are familiar. Dr. Simon, of Singapore, says that, although he may have heard vague reports about such a disease he has never come across a case himself; and his experience has been a very large one, embracing patients from all parts of the Malay Archipelago as well as from China and India. Dr. Bentley, who has practised in Java as well as in Singapore, makes exactly the same statement. Dr. Walker, of Sandakan, Borneo, is not familiar with the disease; he can recall only one case, seen in the convalescent stage, which might have been of this nature. Dr. Atkinson, of the Civil Hospital, Hongkong—a great gathering place for sick people from all parts of the East, as well as for local patients,—and there is much and very severe malarial

disease in Hongkong, or rather in its outskirts—says: "Very frequently the urine contains albumen, and is darker than usual, but I have never met with hæmaturia occurring in a seemingly remittent fever case." Dr. T. Rennie has never met with it in South Formosa or in Foochow; Dr. A. Rennie has never seen it in Tamsui, North Formosa, where malarial fevers are particularly rife. Dr. Jamieson, Shanghai, says: "I have lately gone over my quarter of a century of voluminous observation of cases of malarial fever, and I have been surprised myself by the fact that I have never once noted the occurrence of hæmoglobinuria." As regards my own experience in Formosa, Amoy, and Hongkong, I have never seen what I could be sure was a case of hæmoglobinuric fever. I twice saw hæmoglobinuria in natives in Amoy. The patients were out-patients, and walked to the hospital; so that there could not have been much fever about them. As they only attended once they were lost sight of. I believe they were merely examples of ordinary hæmoglobinuria.

Several French writers allude to the occurrence of hæmoglobinuric fever in Cochin-China; unfortunately, I have not had an opportunity of seeing the original thesis to which they all refer. That some such fever exists there is rendered very probable by the following remarks by Dr. Wenyon, of Fatshan, China: "The fever which ravaged like a plague the Chinese army on the Tonquin border of Kwangsi, in 1885, was frequently accompanied by hæmoglobinuric symptoms; but I was not allowed to deal with or examine medical cases there; the officials told me that I had only been sent up to treat surgical cases. Beyond the fact that some such fever was prevalent and very fatal then, I know little about it. I have seen two or three marked cases in this neighbourhood (Fatshan), but, with one exception, have seen none of these cases more than twice. The exception was a case which I had in hospital three months ago. He was a Hunan man, about 40 years of age, in a low typhoid condition when brought to hospital; temperature, 105°; daily remissions, but for six days never below 101°; urine, port-wine colour, contained both albumen and hæmoglobin, but the quantity of albumen was small. I did not venture to give antipyrin, the man was so weak, but gave quinine and tincture of bark. On the sixth day the temperature was normal, urine of a natural colour, and the man felt so much better that, in spite of persuasion, he left the hospital."

I think, therefore, that although hæmoglobinuric fever,

or a disease in some respects resembling it, may be found in one or two places in Asia, it is, to say the least, exceedingly rare in most of the highly malarious regions there, in fact, practically unknown.

Second. The second epidemiological circumstance pointing to specific differences between ordinary malaria and the poison causing hæmoglobinuric fever is this:—The number of Europeans in India, China, and the East generally is very considerable, and every year there are hundreds who return to England and to Europe suffering from different forms of fever and malarial disease. I have never heard of, read of, or seen an instance of hæmoglobinuric fever among these Anglo-Eastern invalids. In tropical Africa the number of Europeans is comparatively small, and the number of invalids returning to Europe from that country insignificant as compared to those returning from the East. Nevertheless, in my own very limited experience I have seen in England two cases of hæmoglobinuric fever in Anglo-Africans, and within the last few months I have heard of at least half-a-dozen other and similar cases; in fact, it would seem to be by no means an uncommon occurrence.

In France we note exactly the same thing. Every year multitudes of invalids return to that country from Cochin-China and Tonquin and other French possessions in the East—many of them highly malarious; but yet there is no record, as far as I know, of a single case of hæmoglobinuric fever developing in France among these Franco-Eastern invalids. But I can refer to at least five cases in recent French literature in which hæmoglobinuric fever developed in Frenchmen who had returned to France after passing some time in Africa. Bérenger-Féraud records two (*Arch. de Méd. Nav.*, Oct. 1882), one of the cases occurring six or seven months after the patient had returned to France from Mayotte; the other three months after return from Senegal. Rouvier (quoted by Corre) records a similar case;—a soldier who developed the disease in Toulon after serving four years in Senegal. Finally, Kelsch and Kiener detail a fifth case which they observed in Paris in the person of an African traveller who, returning to France in January 1883 developed a series of attacks of hæmoglobinuric fever the following May.

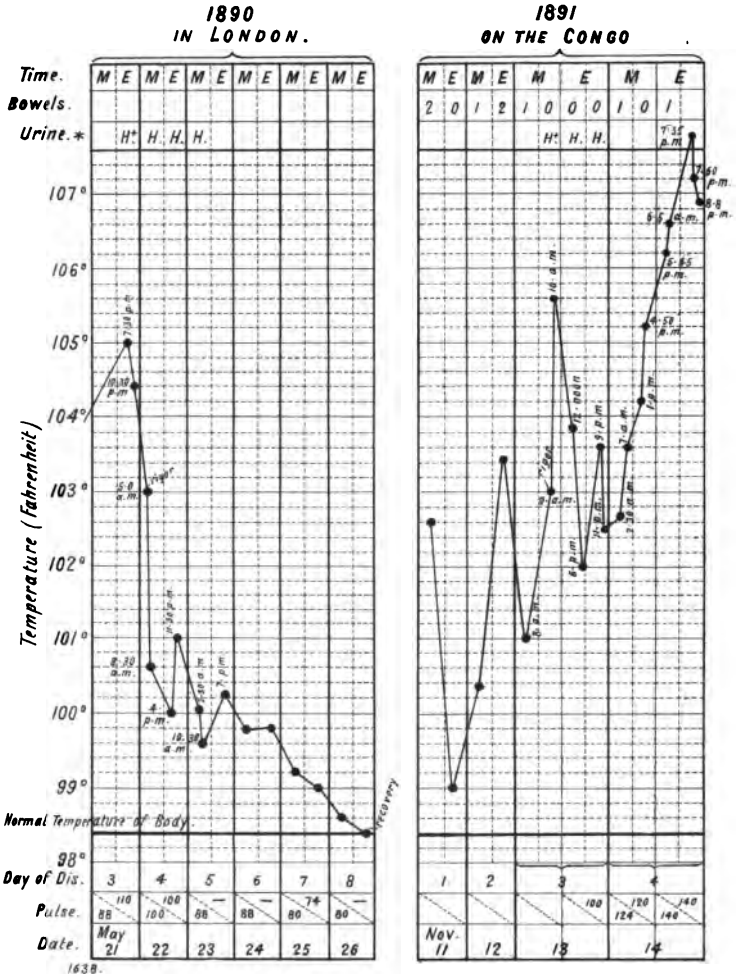
Besides the English cases of which I had personal cognizance, I can refer to four other instances of hæmoglobinuric fever of African origin developing in this country. One case is mentioned in Crosse's book. The

patient while in Africa had attacks of hæmoglobinuric fever in December 1890, and again in March 1891. He then returned to England, and in August of that year, while at Eastbourne, had another attack described as "simple hæmaturia". Another case was alluded to by Dr. Samuel West at the meeting of the Pathological Society on the 31st January last; the patient was under his care; the disease developed in London, and proved fatal.

The two cases which came under my own observation, and to which I have already alluded in some detail, occurred within a few days of landing in England, and about a month after the patients had left the African endemic area. They need not be further alluded to at present; but as the subject is one of some novelty, as well as of importance, I shall add a *précis* of the notes of two other cases which have come under my notice indirectly. For the notes of the first of these I am indebted to Dr. Grattan Guinness, and for those of the second to the patient himself, and to Dr. Hadden, of Dublin.

Mr. N. (Chart I), a missionary, three-and-a-half years on the Lower Congo, at a station some 180 miles up from the mouth of the river, about the end of March 1890 started for England on furlough. On his way down country he was very feverish and had to lay up *en route* at one of the mission-stations with a smart attack of what was considered to be ordinary malarial fever. No sooner had he recovered somewhat than he was called on to nurse a fellow-traveller, a lady, during a severe attack of hæmoglobinuric fever of which she died. On board steamer he was fairly well, only suffering from the cold weather experienced after passing Madeira. The night he landed at Southampton it was cold and raining, and to a chill caught then he attributes an attack of fever that evening. This was on the 19th of May. On the morning of the 20th he had so far recovered as to be able to move about a good deal in London. The weather was cold at the time, and he felt chilled. The same evening he had a severe rigor, lasting about three-quarters of an hour. Before and after the occurrence of the rigor he had taken quinine, and, also, after the rigor, fifteen grains of antipyrine. On the morning of the 21st May he felt fairly well, but during the course of the afternoon he had a recurrence of rigor, and when Dr. Guinness saw him at 7 P.M. he was passing into the hot stage of the fever. His pulse was 110, and his urine was high-coloured,

CHART Nº 1. CHART Nº 2.



*H indicates the occurence of Haemoglobinuria.

depositing an abundant sediment of urates, but no trace of blood or hæmoglobin was recognised. Quarter of an hour later urine was again voided, and now, for the first time, contained blood, or, rather, hæmoglobin. At this time his temperature was 105°, and his skin, though warm, was neither harsh, nor dry, nor perspiring. He complained of aching of the loins and heaviness of the head. At 9 P.M. he began to perspire freely, but his temperature still remained high—105°, his pulse hard and bounding, and his urine was dark from hæmoglobin. At 10.30 P.M. temperature had fallen slightly to 104.4°, and he was dull and heavy-looking. Shortly after midnight he had a copious motion after an enema; his temperature then fell to 103°, and he perspired freely. About 4 A.M. he had another rigor, but temperature did not rise, and perspiration became profuse. It was then noticed that his skin and scleræ were icteric. At this time the patient became very desponding and thought he was going to die. His urine was still very dark, and was passed with pain, and frequently. Temperature, however, steadily fell, and by the evening of that day he felt better. After a restless night, on May 23rd the urine was still dark and albuminous, and was passed with some discomfort; but towards evening it had cleared up in great measure, and the yellow colour of the skin was less decided. The temperature was then only 100°. The note on May 24th is to the effect that he had passed a good night, and that he improved further during the day. After this date there was no return of the fever, and the patient gradually regained his usual health. During the attack he was treated with liberal doses of quinine, to the amount of eleven grains on the 20th May, thirty grains on the 21st, and sixty grains on the 22nd. He had also several doses of gallic acid, besides purgatives.

Unfortunately, the history of this case does not stop here. In May of the following year Mr. N. returned to the Congo. During the first few months he kept well, and it was not until September that he began to get fever again, and then it was only a slight attack lasting a couple of days or so. He was careless in exposing himself to the sun and weather, and he worked very hard. About the beginning of November he complained of feeling tired, sleepless, and without appetite, but still he persisted in working and going about. On November 11th he began to get fever of a remittent character. On the 13th hæmoglobinuria set in, and on the evening of the following day

he died, urine having been suppressed for nearly twenty-four hours, and the temperature having risen to 107.8° (Chart II). During this attack, as on the previous occasion while in England, he was liberally dosed with quinine.

Another missionary who had suffered from hæmoglobinuric fever in Africa informed me that he had lived in the Congo country from April 1889 till the summer of 1892, when he returned to England. During his residence in Africa he had frequent attacks of fever. One attack, which may have been typhoid, was more severe than the others, as it laid him up for three or four weeks; the other attacks lasted only a day or two. Just before leaving for England he had two attacks of what he calls "intermittent", but on leaving the Congo on 10th June 1892, and for a fortnight afterwards, he was quite well. On his way up the African coast he contracted dysentery at Lagos, and during the remainder of the voyage he was very ill. For a week before arriving in England he had attacks of irregular feverishness, chills, and vomiting, but he saw no sign of blood in his urine. He arrived in England on 23rd July. On the evenings of the 25th, 26th, and 28th he had fever, but he was well enough to be about on the 29th. Three weeks later, on the 20th August, being then in Ireland, he believes he caught a chill. Next day, finding that his temperature at 1 P.M. had run up to 103°, he went to bed and took a purgative and a hot drink. By 7 or 8 in the evening he had perspired freely. He then took fifteen grains of quinine and fell asleep. About 9 o'clock he woke up feeling chilly and very ill. Vomiting and severe rigor then set in. Dr. Hadden of Dublin, who saw the patient, describes the shivering as "the most alarming and violent rigor he had ever witnessed". By midnight the patient appeared to Dr. Hadden to be dying, his pulse being scarcely perceptible at the wrist, and his temperature over 104°. The urine passed an hour before was of a brownish black colour, had a distinct sediment, and coagulated on boiling. Warm bottles were applied to the body, and gradually the violence of the rigor abated and the patient's condition improved. In the morning he himself noticed that his urine was dark-coloured, and Dr. Hadden ascertained that it still contained albumen. By evening, however, the fever had subsided, and in a few days the urine had quite cleared up, and the patient was about as usual. There has been no recurrence of the fever or of the hæmoglobinuria, and when I examined the urine a month ago it was perfectly normal.

Besides these six English cases I have heard of others, but cannot supply particulars. Disregarding them, but including the French cases already referred to, we have the record of eleven well-authenticated examples of hæmoglobinuric fever which have occurred comparatively recently in France and England in Europeans who had resided for some time in Africa. Although I have been on the outlook for such cases, I have not seen or heard of anything similar in anyone from India, China, or elsewhere in the East.

Third. With regard to the first part of the third proposition advanced, viz., that there is no distinct account of hæmoglobinuric fever in medical literature prior to 1850, I can only say that, with the exception of one short passage in Boyle's *Practical Medico-Historical Account of the Western Coast of Africa,* published in London in 1831, I can find no allusion in medical literature prior to the year mentioned which might be construed as referring to this affection. And even this possible allusion by Boyle is in a sense second-hand, for it is quoted from a report by Tidlie, written in 1822, on the *Epidemic Fever of the West Coast,* and all that it says on the subject is that sometimes "the urine has the appearance of bloody water". It is very strange that a condition so alarming, so unusual in ordinary fevers, and one so calculated to force itself on the attention, should have been systematically overlooked by generation after generation of medical men, had it been in former days at all common, or anything like so common as it is at present.

In a valuable thesis on the *West African Fever*, by Dr. Battersby, which I have had the privilege of reading, the following passage occurs: "It is hard for anyone who is familiar with the fever to believe that this prominent symptom" (referring to the hæmoglobinuria) "could have been overlooked, as its appearances are so characteristic, and the course of the disease so defined, that it is difficult to make a mistake in diagnosis." I think it very probable that this absence of allusion to Blackwater fever until recent years receives its explanation in the second part of my third proposition, which is to the effect that there is evidence that of late years the endemic area of this disease has extended. Positive evidence to this effect is wanting as regards Africa, but it is forthcoming as regards America, and can be found in the medical journals of the Southern States of the Union. I am sorry that, owing to difficulties of reference, I have been unable personally to

go over this evidence in detail, but it has been carefully studied by Hirsch, who distinctly says, in his *Geographical and Historical Pathology*, under the heading of "New Types", that hæmaturic fever is really a new disease, or, rather, according to his view, a new form of malarial disease. He is very positive about its recent extension in the United States, and quotes many American writers in support of his allegation. Hirsch is a most careful and critical writer, and one not likely to fall into error in such a matter. Now, if hæmoglobinuric fever has extended in America within recent times, is it not reasonable to explain the silence of the older writers on African disease by the supposition that the appearance of hæmoglobinuric fever on the West Coast of Africa is but a comparatively modern event. Dr. Battersby, who has seen much of the disease on the Niger, and, moreover, has had personal experience of it, tells me that he thinks this formidable affection is becoming year by year more prevalent in this part of Africa.

From these, and from other considerations, I think that there is good *primâ facie* evidence for the truth of my conjecture that hæmoglobinuric fever is not simply a form of ordinary malarial fever, but that it is dependent on a poison which, though resembling in some of its effects ordinary malaria, differs from it in other respects very materially. Whether this difference is, in a biological sense, a specific one, or only of the nature of a variety, I cannot say; nor shall we be able to pronounce on this until our knowledge of the malaria-germ itself has extended very considerably; but certain it is that there are strong clinical, historical, and epidemiological grounds for believing that these two morbid states are neither etiologically nor pathologically identical.

Thinking I might get some information on the subject from direct observation of any germ which might be present in the blood in hæmoglobinuric fever, I made two prolonged examinations of the blood of the patient whose case I describe at the beginning of this paper. I searched many slides of his blood on two occasions, each examination lasting perhaps for a couple of hours, and carried out in conformity with Laveran's directions. But I cannot say positively that on either occasion I saw unquestionable malaria plasmodia. There were certainly no crescents and no flagellated organisms present. I did see, however, three bodies which possibly were, and which answered in a rough way to the description of two of the forms of Laveran's bodies. In two of the instances they

appeared to be intracorpuscular and were spherical or discoid in shape, occupying the whole of a corpuscle with the exception of a narrow rim of normally-coloured hæmoglobin. They were colourless except at the periphery, which was encircled by a corona of very minute dark pigment-granules. The third body observed had the appearance—obscurely indicated however—described as the "rosette" form of the plasmodium, and was considerably smaller than the other two, occupying perhaps about half only of the corpuscle it lay in. I saw no bodies having amœboid movements, either outside or inside the corpuscles, and no free bodies such as have been so frequently described as characteristic of malarial blood. As regards the intracorpuscular bodies I did see, I cannot avoid the impression that possibly they were the result of changes in the corpuscles of a degenerative character, and in some way a result, and not a cause of the hæmolysis which was in active progress at the time of my examination. It is possible that this absence of parasites, or, assuming that the three bodies I did see were parasites, that this comparative absence of parasites may have been owing to the circumstance that my examinations were made rather late in the fever, as it was not until after the sweating stage had set in, some five hours from the commencement of the initial rigor, that the first examination was made, and the second not until the afternoon of the following day, and, moreover, that the patient had been taking quinine freely. Still, I cannot but think that if hæmoglobinuric fever is caused by the germ reputed to be the cause of malarial fever, and especially if the extensive blood-destruction which I saw in progress was the result of the mechanical presence of the plasmodium malariæ in the blood-cells, as Laveran and others maintain, I ought to have seen the parasite in proportionate abundance, and many examples of them in every field of the microscope. I have come across no observations by others on the blood of hæmoglobinuric fever undertaken with special reference to the presence or absence in this disease of the malarial plasmodia. Such observations are much wanted; but I may remark that before they can be made with sufficient frequency, it will be necessary, in order that the observations and experience of the busy practitioner may be utilised, that the present methods of search be simplified, made more reliable, and, above all, more expeditious. A clinical method for diagnosis which requires one or two hours to apply is practically useless.

I might here remark that, as regards this hæmolysis which occurs both in hæmoglobinuric and in ordinary malarial fever, my view of the matter is that it is not a direct result of the mechanical presence of a plasmodium, or of other protozoal organism in the diseased corpuscles themselves. I have examined blood from cases of Asiatic malarial fever, as well as blood from this hæmoglobinuric fever case, in which not one corpuscle in ten could be considered healthy, and yet the most careful scrutiny with high powers and suitable illumination entirely failed to discover more than two or three bodies which could be interpreted as being Laveran's bodies, and that, too, in the course of examinations lasting not for minutes merely, but for hours. Consequently, I look on the poikilocytosis in these cases as the result of poisoning of the blood by some product, or secondary effect of a disease-germ, and not of the direct mechanical action of the germ itself on each individual distorted corpuscle. The black pigment found in the organs in malaria may be directly evolved from the hæmoglobin by and while the plasmodium is epi- or intra-corpuscular, and be subsequently deposited in the well-known seats of malarial pigmentation; but the prodigiously extensive and often sudden hæmolysis and hæmoglobinæmia and poikilocytosis in some cases of malarial fever are surely the result of chemical poisoning, the hæmoglobin being subsequently deposited in the tissues as the ochre pigment of Kelsch and Kiener, or eliminated by the liver as bile pigment, or by the kidneys as hæmoglobin or hæmoglobin derivatives.

I should like to allude to one other matter which may possibly contribute to throw light on the etiology of this very obscure disease.

Whilst examining the urine of the hæmoglobinuric fever case I have so frequently alluded to, I came across some curious bodies, the nature and signification of which I am at a loss to explain. These bodies I found in the lowest layer of the sediment of tube-casts and granular matter deposited from the porter-coloured urine. They resembled in shape and size the ova of a parasite; but they were evidently not of this nature, as, though frequently occurring singly, they were usually arranged in groups of twos and threes (Figs. 2, 3, 4), the elements lying side by side with their short axes approximated, and not—as they would have been had they come from the uterus of a parasite—with the long axes approximated; very often, too, they were arranged in large bunches or clusters (Fig. 1), looking very

much like the end of a head of Indian corn. The individual bodies were dark reddish brown in colour—harmonising in this respect with the tube-casts and granular pigment matter among which they lay. It is just possible that these bodies were something which had got accidentally mixed with the urine after it was passed; but the way in which their colour harmonised with the other urinary deposits present is against such a supposition. Unlike the tube-casts and brown pigment matter, the oval bodies were not soluble in nitric acid, or liquor potassæ, nor were they affected by alcohol or chloroform. They were fairly uniform in size, measuring about 1-800″ by 1-1000″, or thereabouts. They had a distinct double outline, and, in many of them, at one end indications of an operculum, or, rather, absence of outer wall, were faintly distinguishable. They could not be fractured readily by pressure on the cover-

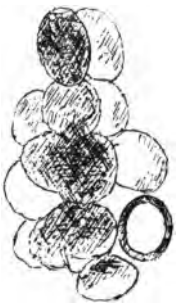


Fig. 1.

Fig. 2.

Fig. 3.

Fig. 4.

glass. I cannot say what was the nature of their contents, as the outer wall or shell was too opaque to admit of this being made out. On examining a specimen of the urine thirty-six hours after it was passed I found, in two examples (Fig. 3) at least, that the contents of these little bodies had escaped through a considerable and circular opening at one pole, and that the ova-like bodies were now hollow and filled with urine. That their original contents had escaped was evident, for I could make out the periphery of the cavity; and in the interior of one I saw a large bacterium moving about, showing that free communication existed between the interior of the body it lay in and the surrounding urine. The idea that they might have been some species of coccidium has occurred to me—perhaps because coccidia are coming into fashion just at present. Whatever their exact nature may have been, they were evidently an

organism of some sort, and not simply hæmoglobin or urinary crystals, and, as I have said, I do not think they were owing to accidental contamination of the urine. Future observers would do well to search for similar bodies in such cases; and when a search is undertaken it must be borne in mind that these bodies are of high specific gravity and rapidly sink to the bottom of the urine, and that therefore they will be present in the very lowest layers only.

Before concluding, there are two highly practical points I shall briefly allude to. The first has reference to the treatment of hæmoglobinuric fever; and I would ask what are the grounds for believing that this disease is amenable to quinine? In going over the literature of the subject, as well as in conversations with many individuals of African experience, I have been struck with the uniformity with which, so soon as fever shows itself in the endemic area of this disease, quinine is given, and generally in very large doses; and also that, notwithstanding this liberal dosing with quinine, how in many instances the fever goes on uninfluenced apparently, and perhaps increases in severity. It not infrequently happens that hæmoglobinuria occurs on the third or fourth day of this treatment, and while the patient is in a state of cinchonism. As regards this disease, as in many of the reputedly malarial fevers which I have read of and seen, I am often tempted to think that quinine, so far from being what it is so often called, our "sheet-anchor", is, on the contrary, a fashionable delusion. There is one thing which is very much wanted in therapeutics at the present day, and that is a scientific statement of the actual value of this drug in many tropical fevers, and a logical marshalling of the data on which much of its reputation is founded.

The other point I would refer to is the possibility of the extension of hæmoglobinuric fever to tropical regions of Asia hitherto exempt. It looks as if hæmoglobinuric fever had originated in Africa, and, like yaws, that it had been carried with the negro to America. That it has not as yet been carried to India and much of the Eastern world is possibly owing to the fact that the set of trade and communication with Africa has not been towards Asiatic countries; and because, when communication has taken place, it has been by slow and circuitous routes, affording time for infective individuals or materials to lose their specific disease-causing properties. But when communication becomes more rapid and more direct, I think it does not require much prescience to foretell that there will

ensue an infection of Asiatic soil with African hæmoglobinuric fever-germs, and that in time this disease will establish itself and spread on the Asiatic continent. If the hæmoglobinuric fever-germ is allied to the malarial fever-germ, as the latter has been so the former may be transported to virgin soil. Who can tell what will be the effect in the dissemination of such diseases of such a revolutionising influence on the trade routes of the world as the successful opening of the Panama Canal? A direct trade in fast steamers would immediately ensue between Panama and Hongkong, Manila, Singapore, and India. At present there is no direct trade between tropical America and these places. But the time will come when Panama and the West Indies will have direct communication with the great ports of Eastern Asia, when trade will no longer follow the circuitous route *viâ* San Francisco and Japan, but will proceed by the shorter and more direct route of a few days only across the Pacific. When this comes about the time may not be very far distant when African and American diseases will appear in Asia, and among them hæmoglobinuric fever, and also the somewhat similar but more formidable yellow fever.

VARIOLA AND VACCINIA: THEIR MANIFESTATIONS AND INTER-RELATIONS IN THE LOWER ANIMALS.

AN EXPERIMENTAL RESEARCH.

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(*Read: April* 19*th*, 1893.)

IN the course of certain experiments on the bacteriology of vaccine lymph, an account of which I had the honour of bringing before this Society last year,* I was confronted by an insuperable difficulty (as it then appeared) in the practical testing of certain of the results of my work. Continuous experimentation on children being obviously out of the question, I was naturally led to turn my attention to the discovery, if possible, of some one or more of the lower animals, which by reason of their passing through the various stages of vaccination, and more especially variolation, in a manner comparable with that witnessed in the human subject, might serve me for control experiments.

With this object in view I carefully looked up all the available literature on the subject, but the result of such search, unfortunately, was not encouraging.

In the attempt to give experimental confirmation to the theory of Jenner, who arguing from the prophylactic effects of vaccine against human small-pox, termed cow-pox variola vaccinæ, or small-pox of the cow, numerous observers, including Thiele, McMichael, Sonderland, Ceely, Badcock, Martin and Reiter, and, in more recent times, Voigt, Hime, Haccius, Klein, and others, have inoculated animals of the bovine species with human variolous lymph. In a considerable number of these experiments, however, no local result has apparently been obtained; and even in those cases which have been regarded by their authors as successful, the result of primary transmission has borne

* *Transactions of the International Congress of Hygiene*, London, 1891; and *Transactions of the Epidemiological Society*, 1892.

little resemblance, either in the appearance at the site of inoculation or in the accompanying symptoms, to small-pox as witnessed in the human subject. In point of fact, so wide has been the divergence, that the result obtained has been looked upon by these observers as a transformation rather than an attenuation of variola, and as therefore to be more properly termed variolo-vaccine rather than variola. In other words, such a modification of variola is apparently produced by its transference to bovines that the resulting local affection cannot be distinguished from ordinary cow-pox or vaccinia.*

Although it should be stated that such an interpretation of the results thus obtainable has been strenuously called in question by Chauveau, and by others following in his footsteps, still the fact remains that the total effects obtainable by variolation of these animals bear so little resemblance to human variola, local or general, as to render them useless for the immediate purpose of my own experiments.

In many animals, among which may be mentioned horses, pigs, and dogs, a local effect, passing in greater or less degree through the stages of papule, vesicle, and pustule, can be obtained as the result of inoculation with vaccine lymph. Thus Chauveau, after experiment by subcutaneous and intravascular injection of vaccine lymph, arrived at the conclusion that horse-pox and cow-pox are one and the same disease. In these animals, however, as is found among bovines, the induced vaccinia generally runs a shorter course than in the human subject, while variolation of them rarely or never succeeds.

In addition, I have experimented with vaccinia on rabbits, guinea-pigs, and rats, but as yet with no very definite results.

This being so, I turned my attention to the monkey tribe, on account of their similarity in many respects to man, although assured on high authority that they were not susceptible to either vaccinia or variola. On putting the matter to the test, however, I was agreeably surprised to find that this was not the case, the inoculation of vaccine and of variolous lymph having each of them given, in my hands, successful results in every instance in which I have tried it on the monkey. Briefly described, the *modus operandi* has been as follows: The upper arm, or occasionally the inner surface of the thigh, is shaved on both sides of the body; the skin is then washed with a solution of some disinfectant, such as corrosive sublimate or carbolic acid, and afterwards with alcohol. Each arm (or thigh) is

* To this subject it will be necessary to return in a description of a further stage of my research.

then scarified in three or four places and the lymph well rubbed in.

In the first series of experiments I used ether as an anæsthetic, but I afterwards found this quite unnecessary, as the monkey appears by no means to dislike the scratching process, becoming absolutely quiet as soon as the operation is commenced, and remaining with limbs limp and eyes half closed, as if hypnotized, until its termination, when it at once becomes again as lively as ever.

In the case alike of variola and of vaccinia the local result of inoculation attains its acme (*quâ* vesiculation) in the monkey, as in the human being, about the eighth day. The first signs of reaction appear usually on the third day, by which time, if variolous lymph has been used, there is a distinct though very thin crust over the site of inoculation. In the case of vaccinia the appearance of crust at this date is less marked. By the fifth day vesiculation in both cases has generally commenced, this becoming more obvious up to the eighth day, though even then, as is well shown in the drawings, it is much less marked in variolous cases than in those which have been vaccinated, the difference being recognised with the greatest ease. Later the vesicle gives place in each instance to a pustule, by which time there is not infrequently considerable swelling of the skin and subcutaneous tissue and of the nearest lymphatic glands; the pustule gradually dries up and a scab is formed, which is more pronounced in the case of vaccination than variolation, and which falls off some time during the third week, if the monkey has not picked it off before. The chief difference noted between the effects resulting from the local inoculation of these two diseases is, that in the case of variola there is more or less of a crust from the first; that vesiculation is less marked than in vaccination; that about the ninth to the eleventh day a general eruption may appear, which, in some instances, as in a monkey which was seen by Prof. Foster, covers the whole surface of the body; and that the final scab at the site of inoculation is not so elevated in the variolated as in the vaccinated animal.

In both cases there is usually a rise of body temperature, which is more marked and longer sustained in variola than in vaccinia. After variolation, it was noticed in several instances that the monkey suffered from diarrhœa, that its eyes were suffused, and that it was not as active as usual. A peculiar odour was also noticed, quite distinct from the well-known smell of "monkey".

In no instance had the experiment a fatal termination.

Having thus proved to my own satisfaction that monkeys are susceptible not only to vaccination but also to small-pox, I endeavoured to discover whether any record existed of an epidemic of the latter disease attacking these animals in a state of nature. Mention of such an occurrence, as was pointed out to me, is to be found in the article "Mammalia", in the first edition of Cassell's *Natural History*.

No apparent support having been forthcoming, however, for the statements here made, the account has been omitted, as I was informed by the publishers, from later editions.

Murray, in a pamphlet on Small-pox, Chicken-pox, and Vaccination, published in Melbourne in 1869, also states that "Dr. Jackson has described an epidemic of variola that occurred over New Granada among monkeys". Whether this statement has any greater foundation in fact than the first, I am, however, unable to say.

In his book on Variola and Vaccinia, I find that Buist of Edinburgh describes the effects of variolation of monkeys, and gives plates showing the results he obtained, but he does not appear to have made trial of vaccine lymph in similar fashion.

I next determined to make trial as to the protection against small-pox afforded in the monkey by previous vaccination, and the protection against vaccination afforded it by variolation, and I went on to compare the effect produced by the use of human and of calf vaccine respectively. For this purpose humanized lymph was obtained from Birmingham, where, to the best of my belief, the same strain has been continuously carried on by means of arm-to-arm vaccination for the past thirty-eight years. The calf lymph used was obtained from the Government Animal Vaccination Station in Lamb's Conduit Street, while small-pox lymph was supplied to me from the Hospital Ships, from Warrington, and from Manchester.

The following experiments will serve as illustrations of the system I pursued:—

Experiment 1.—On July 13th, 1892, I vaccinated a male rhæsus monkey in four places on the left arm with calf lymph, on points taken at the A. V. E. on the previous day. On July 20th, the eighth day, the appearance presented was undistinguishable from that of a successful case of human vaccination.

On July 23rd the vesicles had given place to four large scabs raised nearly one-eighth of an inch above the surface of the arm, while the surrounding inflammatory

zone had nearly disappeared. The axillary glands on the same side were considerably enlarged. The arm was drawn on this day by Mr. Lapidge.

By August 9th the scabs had all come off and the monkey was again vaccinated, but this time on the opposite arm in two places, and also on the inside of the right thigh in two places also, with humanized lymph of ascertained activity. The animal was carefully examined day by day up to August 17th, but no sign of the second vaccination having "taken" was observed.

Experiment 2.—On July 19th a large female rhæsus monkey was inoculated by scarification in eight places (four on each arm) with two tubes of somewhat opaque S. P. lymph from the Hospital Ships. It was obtained from a patient *æt.* 19, stated to have been vaccinated in infancy, who was suffering from a semi-confluent attack of the disease. The lymph had been sealed up in carefully sterilized tubes. On July 23rd (the fifth day), the right arm showed papulation and commencing vesiculation. The glands slightly enlarged; left arm not so good. The lymph from which this arm had been done had coagulated in the tube, and very little could be got out. On July 28th a drawing was made by Mr. Lapidge, and on the following day the animal was seen by Dr. Thorne Thorne, Mr. Power, and Dr. Sherrington. On August 18th, a month after inoculation, it was vaccinated in four places on the inner aspect of the right thigh with A. V. E. lymph from calf No. 2809. No result of any kind followed the operation.

Not to weary you with details of the numerous experiments which I have performed on similar lines at intervals of one to five months after the primary inoculation, whether vaccinal or variolous, I may perhaps briefly show, by means of a table,* the general method of experimentation.

1. V. with	H. L.	...	...	Rv. with	C. L.
2. V. „	H. L.	...	...	Rv. „	V. L.
3. V. „	H. L.	...	...	Rv. „	H. L.
4. V. „	C. L.	...	..	Rv. „	H. L.
5. V. „	C. L.	...	...	Rv. „	V. L.
6. V. „	C. L.	...	...	Rv. „	C. L.
7. V. „	V. L.	...	...	Rv. „	H. L.
8. V. „	V. L.	...	...	Rv. „	C. L.
9. V. „	V. L.	..	...	Rv. „	V. L.

No. 8 was afterwards again revaccinated on two occasions, first with V. L. and secondly with C. L. In none

* In this table H. L. = Human lymph; C. L. = Calf lymph; V. L. = Variolous lymph; V. = Vaccinated; Rv. = Revaccinated.

of these experiments did anything in the nature of a successful result follow the first or subsequent revaccinations, although in No. 8 the experiments lasted over a period of five months.

From these experiments it would appear that the protective power of lymph obtained from these three different sources, when inoculated on the monkey, is practically identical in all respects.

I desire next to call attention to the fact that, although protection against subsequent vaccination or inoculation is undoubtedly afforded by the effect produced on the system generally, as the result of the sequence of events at the site of operation that I have described, yet that these local manifestations are apparently not essential for the production of some protection.

My attention was first called to this possibility when, a year or two ago, I was experimenting with lymph which had been sterilized by heating at a temperature of 60° C. Such lymph not only gave rise to no bacterial colonies in plate cultivations made from it, but also it produced no local effect whatever when calves were vaccinated with it. On the first occasion that this occurred I thought that by chance the particular calf might have been the subject of an unnatural insusceptibility, especially as nothing resulted from a subsequent vaccination of it a little later with lymph, which from its effect on other calves and on children was obviously of normal potency. But on repeating the experiment on other calves the course of events was invariably similar, so that no doubt remained in my mind that something of the nature of protection had really been afforded by the primary operation in each instance, although nothing in the way of local reaction had been perceptible.

A similar course of events has been observed by Chauveau, Klein, and myself, in the course of variolation experiments on the calf.

By the introduction of vaccine lymph into the subcutaneous tissue of the back of the monkey, the lymph having previously been diluted with normal saline solution in order to obtain a quantity of fluid easier of manipulation, I find that protection is obtained against subsequent vaccination carried out in the usual manner. In one of the two instances in which I have made trial of this method, a local tumour, possibly an abscess, resulted, probably due to irritation from septic organisms or their products in the lymph.

Whether if glycerinated lymph were used the formation

of such a tumour would be prevented in every instance I am not yet in a position to make any dogmatic assertion.

On looking up Chauveau's work, I find that he has pursued the same method with bovines and horses, and that he confirms me in the opinion that a generalized influence over the system affords (for a time at least) immunity from vaccination obtained without production of local result.

I have also found two instances recorded in recent years in England in which "insusceptibility" to vaccination had apparently been conferred on the child during intra-uterine gestation by an attack of small-pox* in the one case, and by revaccination of the mother in the second. If these cases are trustworthy, such protection must have been afforded through the medium of the blood, or rather of the blood plasma, which alone is capable of diffusion between the maternal and fœtal circulations.

With the hope of throwing some light on this problem, and at the same time making trial of the value of what might possibly afford a new method of protection against small-pox, I devised the following experiment, on somewhat similar lines to the well-known work of Tizzoni and Cantani on tetanus. In a monkey which had been successfully inoculated with variola five months previously, and after an interval of three months had again been variolated and also vaccinated without result, the carotid artery was dissected out and tied with antiseptic precautions, after ætherisation of the animal. A glass canula was then inserted into the artery below the ligature, and about 30 c. c. of blood received into two test tubes, each of which contained a few drops of oxalate solution. The blood which was thus prevented from coagulating was then centrifugalized, and rather more than half the total amount of transparent slightly yellow-tinted plasma was obtained, the red corpuscles remaining in a dense mass at the bottom of the tubes. Of this plasma, about 8 c. c. was then carefully inserted into the peritoneal cavity of a second monkey through a minute incision in the linea alba. Two days after the operation both animals appeared perfectly well.

After an interval of fourteen days, on April 7th, 1893, the second monkey was vaccinated on the left arm and also on the inner aspect of the right thigh with calf lymph on points, obtained from the A. V. E.

I had no opportunity of seeing the animal again until the eighth day, owing to compulsory absence from town, but

* See also Report of Vaccination Committee, Epidemiological Society, 1885-86.

it was then evident that complete protection, at any rate, had certainly not been afforded by the operation.

All the scarified places had "taken", although in each instance the result produced was a somewhat abortive one, as was noticeable on comparing this animal with another which had been vaccinated on the same day and with the same lymph, and which therefore served as an excellent "control".

Some effect had therefore apparently been produced on the system of the monkey by the procedure adopted, but at the same time it was obviously but slight, even though the amount of plasma injected was considerable in relation to the size of the animal. It would appear that the use of the plasma of an immune animal is not likely to afford any result of value sufficient to render it desirable that trial should be made of it on the human subject.

It is conceivable that the oxalate used for the prevention of coagulation may have in some way prevented the effect which otherwise might have been produced on the system, but in view of the fact that Dr. Sherrington has found that leucocytes will live for as long a period as fourteen days in such oxalated plasma, this explanation hardly appears feasible.

Vaccinia and Variola in Bovines and Solipeds.

It is desirable now to consider briefly what is the relationship, if any, which exists between variola and vaccinia. To this end, as a preliminary, let us review the various means by which infection of the animal organism can be brought about experimentally in the case, first, of vaccinia, and afterwards of variola, as in this way only can adequate grounds for a judgment be obtained.

Such experimental methods may be tabulated as follows: —

1. Puncture, incision or scarification of the skin.
2. Injection (*a*) into the cellular tissue, beneath the skin or conjunctiva; (*b*) into the lymphatics; (*c*) into the blood-vessels.
3. Infection through the respiratory tract.
4. Infection through the digestive tract.

With regard to vaccinia, the local results of infection of the skin, more particularly in bovines and the human being, are so well known that it would be a waste of time to enter into any description here. It only remains, therefore, to

call attention to the fact that, as Chauveau has pointed out, a general eruption may follow the vaccination of colts, although unknown as a result of the operation in the case of calves. Accessory vesicles are indeed occasionally seen, but they usually arise at the site of accidental wounds caused by shaving, etc. It is to be remembered also that a spontaneous eruption arising independently of auto-inoculation is not unknown in the human being, as witness the case of his own child, recorded by Dr. Longstaff.

Chauveau has also placed on record a large number of experiments in which he injected vaccine lymph subcutaneously, and also into the lymphatics and blood-vessels of colts, and in a few instances heifers also. With heifers he never obtained any appreciable result, but with colts a generalized eruption followed in four out of eleven cases in which injection was made into the lymphatics, and in eleven out of twenty-seven cases in which the blood-vessels were made the channel of infection. A like effect followed insertion of lymph into a pouch made in the subcutaneous tissue in the neck. The generalized eruption produced in these various ways by the injection of vaccine lymph Chauveau denominates as *horse-pox.*

These experiments as yet I have not had the opportunity of repeating.

That generalized vaccinia can be communicated by means of the *digestive tract* there is considerable evidence to prove, more particularly in the human being. A case is recorded in which M. Cazal of Agde, in 1810, administered to a young girl, apparently refractory to vaccination, a pinch of powdered vaccine crusts in soup, in the hope of obtaining a more definite effect. As a result, constitutional symptoms were observed at the end of six days, which were followed by a general eruption of 180 vesicles all of clearly vaccine type.

Dr. Etienne mentions a case in which a child *æt.* 4 sucked the vesicles on its arm, which had been injured nine days after the operation. Dr. Richard also gives an account of a girl *æt.* 8 years, who sucked the vaccine vesicles on the arm of a younger brother. In both instances a generalized eruption of vesicles followed after an interval of about four days.

More recently somewhat similar cases have been placed on record in this country by Drs. Martin, Acland, Colcott Fox, and others.

Experimentally, a like result was obtained by Chauveau in two colts, which he infected by the addition of vaccine lymph to their drink.

Similarly, variolous infection may be obtained by way of the digestive tract, according to Marsillac,* who states that variolous matter spread between slices of bread and butter was given to two children and to a dog, and that by this means the children as well as the dog suffered in consequence from a very mild attack of small-pox. In this connection attention may also be called to an observation of Ceely's, which is, I believe, but little known. He records† an instance in which five out of eight milch cows sickened with cow-pox within twelve or fourteen days of their having been seen to be licking over a quantity of flock from the bed on which a patient had died of confluent small-pox, and which had been spread out in the field for purification. It is of course possible, however, that infection by way of the respiratory tract may have been a factor also in this case.

Being much struck by perusal of this statement, I endeavoured to imitate the occurrence experimentally. For this purpose I blew out the contents of about a dozen capillary tubes of small-pox lymph (many of them less than half full) which I had had by me for some time, into a small quantity of normal saline solution. This was afterwards diluted to about half a pint with normal saline, and after the addition of some small-pox "seeds" from the Hospital Ships, administered by means of a feeding-bottle to a heifer about two months old. The calf remained apparently well, and presented no symptoms of any sort for some days afterwards, but on March 11th (the tenth day) we found on examination that the mammary gland, which was hardly noticeable at the time of operation, was obviously swollen and "knotted". The swelling increased for the next two days until the mass measured four or five inches across, and then commenced to die away without any eruption having appeared. It was suggested to me that it would be well to repeat the experiment on a cow which had recently calved, and in which, therefore, the mammary gland is fully functional, as in the case of Ceely's cows. This, however, I have had no opportunity of doing up to the present. Subsequent vaccination of this calf induced an eruption of a somewhat abortive character. I also experimented on a fox-terrier dog by feeding it with small-pox crusts from the ships. No result followed, but I afterwards learned

* Quoted by Viborg of Copenhagen, in *Med. and Phys. Journal*, vol. viii, p. 272, 1802.

† "Observations on the Variolæ Vaccinæ," *Transactions of Provincial Med. and Surg. Association*, 1842.

that there was some doubt as to whether the package containing the crusts had not been "disinfected" by mistake before leaving the ships.

The only recorded instances of the *intra-venous* injection of variolous lymph of which I know are to be found in a paper by Dr. Klein* in the Reports of the Medical Officer to the Local Government Board. The paper deals mainly with attempts at variolous inoculation of bovines, carried out in 1878, which at the time were considered to be altogether unsuccessful. Among them Dr. Klein mentions two cases in which lymph previously diluted with normal saline was injected into a subcutaneous vein of the ear. The only result noted was some slight suppuration of the tissues of the ear; but it is to be observed that these injections were each done at an interval of eight days after a previous inoculation by scarification of the skin. As I have already shown in the case of vaccine lymph, and as Chauveau has also shown with regard to variolous inoculation, a certain amount of protection, at any rate, would have resulted from the previous operation, even though that also had brought about no obvious effect.

It should be mentioned, however, that Klein was successful in producing a general eruption in the sheep by means of an intra-venous injection of the lymph from a case of sheep-pox.†

Sonderland of Barmen, in 1830, claimed to have caused infection by way of the *respiratory tract*, but his method of experimentation has failed in the hands of later observers.

On turning, however, to the question of infection from skin inoculation, whether by puncture, incision, or scarification, the literature of the subject becomes so vast as to make it extremely difficult to condense the opinions of the numerous observers within reasonable limits. In consequence of the view, which has received much scientific support from the times of Jenner onwards, that cow-pox represents merely a modification of human small-pox brought about by residence in the tissues of the cow, the experiments to which I now have to refer have almost invariably been carried out on bovines.

It is quite impossible here to do more than mention the names of those who have taken up this line of research, except in the case of one or two of those more recent observers who have engaged in the work during the past few years. I append here a list of such names, placed, as

* Report of Medical Officer to Local Government Board, 1879.

† Rep. of Med. Officer to L. G. B., New Series, No. III, 1874.

far as possible, in chronological order. It is a noteworthy fact that every observer mentioned, with the exception of Chauveau and his colleagues of the Lyons Commission, claims to have obtained positive results as regards the production of typical vaccinia after one or more removes, as the result of variolation of the cow:—

Chronological List of Observers who have carried out Variolation Experiments on Bovines.

1807. Viborg, Copenhagen.
„ Gassner, Gunsburg.
1828. McMichael, Egypt.
1830. Sunderland, Barmen.
„ Numann, Utrecht.
1832. MacPhail, Baltimore.
1836. Thiele, Russia.
„ Martin, Allteborough, Mass.
„ MacPherson, India.
1839. Reiter, Munich.
„ Ceely, England.
1840. Badcock, England.
1863-65. Chauveau, Lyons.
1868. Shortt, India.
„ ? John Greene, Birmingham.
1871. Chauveau, Lyons.
1881. Voigt, Hamburg.
1886-90. Fischer, Carlsruhe.
1889. King, Madras.
1890-91. Eternod and Haccius, Geneva.
1892. Simpson in India, and Hime, Klein, and myself in England.

Although there is so great a unanimity of opinion among those who have worked at this subject, it must be confessed that many of the earlier experiments are practically worthless owing to the conditions under which they were carried out. Some of the main objections are based on the frequently concomitant use of vaccinal and of variolous lymph in the same animal, and the want of care as to the cleanliness and freedom from vaccine contamination of lancet and "points" used in the experiments. A somewhat similar objection might also be urged against much of this work, even that of quite recent date, in that, as it is perhaps not surprising, it should have been carried out for the most part in vaccine establishments and by persons engaged in the practice of vaccination. Such criticism, whatever may be the exact value to be attached to it, would, I believe, hold in the case of most of the experiments on the lines indicated which have been done since the date of the Lyons Commission, with the exception of those which have within the twelve months been carried out by Klein and by myself.

Without doubt, however, the largest amount of research work in this direction during recent years is that of Haccius, the Director of the Swiss Vaccinal Institute. In a work entitled *Variolo-Vaccine*,* which has been recently published, and which is profusely illustrated with beautiful

* *Variolo-Vaccine*, par Ch. Haccius, Genève, 1892.

drawings and photographs, he gives an account of no less than eight successful series of experiments, in each of which a strain of variolous lymph, obtained in the first instance from the human being, was carried on from calf to calf through, in some instances, as many as six or seven removes. The general result was that by the second, or at most the third remove the effect produced was altogether undistinguishable from that which we are accustomed to see in a calf which has been successfully vaccinated.

With the lymph of the fifth or sixth remove a number of previously unprotected children were vaccinated with unfailing success. The resulting vesicles could in no way be distinguished from ordinary vaccination vesicles of equal age. It is particularly stated that every precaution was taken, as, for instance, the sterilization of the lancet before each operation, to prevent the accidental transmission of vaccinia.

The single experiment which was published last year by Dr. Hime of Bradford differs from those of Haccius in that the former observer obtained in the calf, which was directly inoculated with variolous lymph, three vesicles having the appearance and running through the usual course of typical vaccination vesicles.

From the brief account of his experiments, which has been published by Simpson, it would appear that his experience has been very similar to that of Hime.

Concerning Dr. Klein's results I, at present, know but little, for the reason that, as his experiments were carried on concurrently with some of mine, I purposely refrained from seeking information on the point. I took this course, feeling that if it should afterwards appear that we had obtained very similar results, such mutual corroboration would be all the more valuable from a scientific point of view.

My own experiments on this point I now propose to describe as succinctly as possible.

Experiment 1.—On August 11th, 1892, I inoculated a cow-calf, about six weeks old (C), in thirty-two incisions and two scarified patches on the abdomen. For this purpose I made use of two capillary tubes of variolous lymph taken from a vaccinated girl *æt.* 16, a patient at the Hospital Ships, who was suffering from a typical attack of discrete small-pox. She had been admitted on July 26th, and the lymph was taken on July 30th, with antiseptic precautions, into tubes which had been previously sterilized.

When the calf was examined on August 13th nothing

was to be seen, except that a slight scab was forming over the scarified patches. Two days later, however (on August 15th), some of the incisions, more particularly the more posterior ones, looked somewhat red and elevated, while in their course were several small points more distinctly elevated than the rest. On the inner aspect of each thigh, quite apart from any of the incisions, was noticed a crop of shotty and apparently slightly vesicular pimples. On the right side also were a few isolated pimples at some distance from the patch. At this stage the calf was photographed and a drawing made by Mr. Lapidge, which I have brought for your inspection.

On August 17th (the eighth day), with the aid of compression forceps, I scraped three of the incisions, removing lymph and crusts together, with which Calf D was inoculated the same day in fifty-two incisions. To finish the history of Calf C, however, I may state that, in the first place, there was never any appreciable rise of temperature or apparent illness; that by August 19th the eruption was commencing to crust over; and, finally, that rather more than a month later (on September 22nd) I vaccinated in twenty-three long incisions with calf-lymph obtained from the A. V. E., but without producing any result whatsoever.

Experiment 2.—On August 17th a cow-calf (D), two months old, was inoculated in fifty-six linear scarifications with lymph and crust obtained from the previously-mentioned incisions of Calf C. Two days later it was obvious that the experiment would be successful, as the lines of incision were all distinctly raised and surrounded by a delicate pink flush.

On August 20th (the fourth day) all the incisions had evidently "taken" well, the areola around each being now about ⅛ inch wide. On the same day this calf was photographed, and another, Calf E, inoculated from it. It was also drawn in colours by Mr. Lapidge. A month later (on September 22nd) it (D) was vaccinated in seventeen incisions, each about two inches in length, with calf-lymph obtained from the A. V. E. Again the result was absolutely negative.

Experiment 3.—On August 20th, 1892, a small cow-calf (E), seven weeks old, was inoculated in twenty-seven linear incisions from Calf D with both lymph and crusts. In this instance, again, every incision had "taken" on the fourth day, when another drawing was made of the appearances presented. On August 25th some of the "places" were distinctly vesicular along their margins.

For reasons of economy the series was not continued further, and although some tubes of lymph were collected from this calf, I did not feel justified, without further experience, in trying its effect on children. Unfortunately, I had not fully appreciated at this time the possibility of using monkeys for purposes of control.

Experiment 4.—On November 29th, 1892, I inoculated a calf (F) in thirty-seven incisions and one scarified patch with five tubes of variolous lymph obtained from a case of confluent small-pox in an unvaccinated child *æt.* 3 years at Warrington. As no result followed, I inoculated again on the ninth day with a further supply of lymph from Warrington, in the hope of obtaining Ceely's result in the revivification of the former incisions. Again, however, I was doomed to disappointment.

Experiment 5.—A young cow calf (G) was inoculated on December 12th, 1892, in forty-eight linear incisions, with Warrington lymph from a case of confluent small-pox in an unvaccinated man aged twenty-three.

On December 15th a slight blush was visible at the site of all the incisions, and several little "shotty" points were noticeable to the finger when pressed over the skin, particularly on the inner surface of the right thigh. On the evening of the same day I was unfortunately attacked by an illness which confined me to hospital for nearly a month, so that I had no opportunity of observing the further progress of this case, which, apparently, gave every promise of success.

Experiment 6.—The last experiment of this nature which I have performed, and of which the result is shown in a photograph, need not be related in detail, as owing to pressure of other work I was unable to get back to town before what had evidently been minute vesicles on the tract of some of the posterior incisions had practically dried up. As a matter of fact, another calf was inoculated from this one, but did not "take", possibly in part for the reason that it was extremely young, having to be fed on milk entirely, and because it was suffering from a severe attack of diarrhœa at the time.

Thus far, then, I have obtained an undoubtedly successful result in one case only out of four attempts; but I have at any rate been able to satisfy myself that it is possible to variolate the calf; and further, that the result obtained in the first instance becomes greatly modified in the course of successive removes; and again, that animals which have been thus treated are no longer susceptible to vaccination.

I may mention here that, by way of precaution, the scalpels used were invariably first carefully sterilized in a flame; that, after use, the table was thoroughly washed with carbolic acid and hot water, and during the intervals of use kept exposed to the open air.

In none of my experiments, then, did I obtain anything resembling a true vaccine vesicle in the calf first inoculated, as happened in Simpson and Hime's cases. On the other hand, I must say that I have never yet met with the precise appearances described by Chauveau in the Report of the Lyons Commission. How these discrepancies are to be explained it seems impossible to say as yet, but I hope that by making trial under varying conditions I may hereafter be enabled to solve the problem. As far as can be judged from what I have done at present, I find myself more in agreement with Haccius, whose variolo-vaccine lymph, as he calls it, has now been carried through many generations of children without producing any of the ill effects of variolous inoculation.

Those who deny the relationship of small-pox and cow-pox will say that these children have been variolated and not vaccinated. One, of course, admits that they *have* been variolated, in the sense that they have been inoculated with lymph descended from a case of human small-pox, just as was probably the case in the enormous number of children on whom Badcock's lymph was used, but differing from the mild inoculations of Adam Dimsdale and the Suttons in that the resulting disease is no longer contagious. Such procedure is also strictly comparable with those methods of protective inoculation by the use of attenuated virus, which of late years have given such valuable results in the prevention and treatment of various zymotic diseases. If, then, it can be conclusively proved that small-pox lymph, by passage through the system of the calf, can be so attenuated and altered in character as to become deprived of its power of causing a generalized eruption, and, more important still, that by such treatment it loses its contagious nature, while causing at the site of inoculation what is undistinguishable from a typical vaccine vesicle, it is, I think, difficult to find any ground for the assertion that vaccinia is not a modification of, if not identical with, variola, especially as these two diseases exert a mutually protective action against one another. On the other hand, as I have abundantly shown in an earlier section of this paper, vaccinia, when passed through the organism of animals other than the cow, is capable in certain

cases of so far regaining its virulence as to give rise again to a generalized eruption.

I am aware that Crookshank and others assert that this power of mutual protection is no argument, for the reason that there are several diseases which, when inoculated, cause a local effect somewhat similar to that produced by variolation or vaccination, and which exert a so-called temporary antagonism against small-pox.

This question the time at my disposal on the present occasion will, unfortunately, not allow me to discuss, but I must confess that up to the present I have seen nothing adduced in the way of evidence which would lead me to the conviction that these two diseases, which protect against one another, are yet absolutely dissimilar in nature, such a state of things being altogether opposed to what we at present know of the natural history of infectious diseases. In any case such statements should, I think, be received with all reserve, unless supported by an amount of trustworthy experimental evidence, far in excess of any that is at present forthcoming.

Bacteriology of Vaccine Lymph.

I desire now to turn to a branch of my subject which I have had the honour on a previous occasion of bringing, in part, before the notice of this Society. I refer to the study of the bacteriology of vaccine lymph, and to the lessons which may be learnt from such a study, as to the means of storage best adapted for securing sustained purity of the lymph and the unimpaired manifestation for indefinite periods of the action peculiar and essential to its use.

In the volume recently published of the *Transactions* of the Bacteriological Section of the Hygiene Congress, held in London in August 1891, will be found two papers dealing to a greater or less extent with this subject; the first by myself, the second by Professor Crookshank. Although working quite independently, we both arrived at the conclusion, in which we are corroborated by Pfeiffer and many other observers, that although numerous bacteria can be grown in various nutrient media from specimens of vaccine lymph obtained in the ordinary way, yet that to none of these could be assigned the *rôle* of the actual vaccine virus, which as yet remains unidentified. For this reason I had assigned to these bacteria the term "extraneous", signifying thereby that their presence is not in any way

essential to the successful action of the vaccine lymph. In this also Professor Crookshank agrees with me, for he says: "None of these different species of bacteria are peculiar to vaccine lymph; there is no bacterium constantly present in human and calf vaccine, and there is not one which can be regarded as the contagium. To sum up, most of them are well-known saprophytic bacteria, and some are identical with bacteria commonly found in suppuration. Vaccine lymph is a most suitable cultivating medium for micro-organisms, and bacteria invariably get access to the contents of the vaccine vesicle."

A lengthy list is given by Crookshank of the various bacteria which may be isolated from human or calf lymph by the method of plate cultivations, but he does not state whether any and, if so, what precautions had been taken with regard to the collection of the lymph with which he experimented; neither does he attempt to distinguish between those bacteria which are commonly to be found, and those whose presence is exceptional. I have shown, however, that there are three species of micro-organisms, one or other, or all, of which is almost universally to be found in every specimen of vaccine lymph examined, of which one, the staphylococcus albus, is usually to be found in the upper layers of healthy skin. Of more importance is the fact that in certain cases, though rarely, I have been able to satisfy myself as to the presence of the streptococcus pyogenes, and, moreover, it is on record in certainly one instance at least that the streptococcus of erysipelas has also been isolated from a specimen of vaccine lymph.

That untoward results should occasionally, in certain cases, follow the inoculation during the act of vaccination of one or other of the various extraneous organisms which may be present in the lymph employed is not to be wondered at; indeed, I take it that it is rather a matter for wonder that the evil results following the present somewhat empirical practice of vaccination have been, in the past, so few in proportion to the vast numbers that have undergone the operation. Still, in view of the feeling against vaccination which is prevalent at the present time, it is most desirable that we should not, if it be possible to avoid it, run any risk of performing a septic inoculation on a patient under the guise of vaccination.

If only it had been possible to isolate the contagium of vaccinia (or variola), and to carry on, without loss of specificity, pure cultures of it in some nutrient medium from generation to generation, this portion of the problem would

be solved; but, although the number of observers who have turned their attention to this point is legion, and although a claim is every now and again advanced, success cannot as yet be said to have been obtained.

Fortunately, however, we have at our disposal other means of satisfactorily ensuring the purity of vaccine lymph.

Some two years ago, when experimenting on the possibility of isolating the specific contagium of vaccinia and variola, it struck me that the exuberant growth of evidently "extraneous" organisms, which I obtained in all the various nutrient media employed, might be capable of superseding the more important organism for which I was seeking. I therefore turned my attention to the discovery, if possible, of some means of treating vaccine lymph which should inhibit all extraneous organisms without injuring its potency for vaccination.

Another point which directed my research work at that time in the direction I have indicated, was that my attention was called to the opacity which commonly occurs after a longer or shorter period in lymph which has been stored in sealed capillary tubes, and to the deterioration in activity of the lymph which is found to be a concomitant of such opacity.

In former papers I have shown that this opacity of old stored lymph is quite independent of any coagulation in the lymph, as no coagulum was found on breaking many of the tubes in which it was most marked. Further, I have shown that if cultivation experiments are carried out with the contents of tubes which have become opaque, and also simultaneously, for purposes of control, from tubes of comparatively fresh lymph, many more colonies result in the plates poured from inoculations of the old tubes than in those for which more recent lymph is used. I concluded, therefore, that we are apparently justified in considering that the opacity of old stored lymph is, in the main, the outcome of an enormous multiplication of aërobic bacteria, the ancestors of which were present in the lymph when first taken, although their numbers are then so comparatively small as not to render it in any way turbid. These evidently find in the lymph, especially when removed from the body, a suitable medium for their subsequent multiplication, while at the same time it would appear that such growth has the result of gradually inhibiting the specific effect proper to the vaccine virus itself.

In this case also, then, the obvious indication was not

only to prevent such multiplication of extraneous organisms subsequent to storage in the usual manner, but, if possible, to remove them altogether without injury to the actual contagium of vaccinia.

Without detailing the various experiments which were carried out with this object in view, a full account of which I have already published, it is necessary in this place to state briefly the lines on which the work was carried out. In the first place I made trial of the method of fractional heating, which had, in the hands of Kitasato, met with such brilliant success in the isolation of the bacillus of tetanus. Proceeding in this manner, and in every experiment observing the precaution of making control cultures, I presently arrived at a temperature exposure to which is apparently incompatible with the continued existence of those micro-organisms which can ordinarily be grown when vaccine lymph is inoculated into nutrient jelly. This required temperature ranged between 38° C. and 42° C.; but whereas, after exposure for an hour at the lower register, a few points of growth are occasionally seen in plate cultivations after the lapse of a day or so, while the higher temperature sometimes appeared to exert an injurious effect on the lymph, as far as regards the normal vesiculation which should result from its inoculation in the living animal, I sought for some method of readier application and requiring less delicate manipulation. This I at length found in the admixture with the lymph of a definite proportion of 75 per cent. glycerine in distilled and sterilized water prior to storage in capillary tubes, which latter had been sterilized by heat.

Many years ago Müller showed that lymph might be diluted with three times its bulk of such a mixture and still retain its properties unimpaired, a fact which has been taken advantage of at many of the continental vaccine stations, and by more than one purveyor of trade lymph. An argument in favour of the use of lymph diluted in this way with glycerine is found in the fact that such a mixture does not dry up nearly as readily as ordinary lymph, and, therefore, in the hands of operators all but the most expert, affords greater facilities towards the attainment of a uniformly successful series of vaccinations. The fact also that a much larger supply of lymph is thus made available is so obvious that it needs not to be insisted on.

Not only is lymph thus treated efficient as vaccine in the old sense of the word, but, as time goes on, instead of losing its effect on inoculation, its potency actually becomes in-

creased. Experiment shows also that in tubes filled with such diluted lymph opacity does not apparently result. As I have previously stated—an observation, by the way, for which I may fairly claim priority—the glycerine inhibits the growth of, and, after a longer or shorter interval, kills off altogether, those aërobic bacteria which I have termed "extraneous". This effect may be demonstrated by making from tubes of glycerinated lymph a series of plate cultivations at gradually increasing intervals of time, together with control cultivations from tubes of untreated lymph. (Photographs of such plates I show you to-night.)

With the assistance of Dr. Cobbett I have also carried out a series of glycerine experiments on a larger scale, not only with the organisms which can be grown from vaccine lymph, but also with numerous other species of bacteria, both pathogenic and saprophytic in nature. With details of these experiments, which we shall hope to publish shortly, I need not detain you now. I will here merely state that the net outcome of our work appears to show that while some pathogenic organisms remain active in admixtures of broth and glycerine, or even in pure glycerine, for longer or shorter periods, other pathogenic, and, as far as our experiments go, all saprophytic, organisms are killed out in from three or four days to as many weeks.

At the time of writing I have seen, for the first time, a paper (dated September 1892) by Achille Sclavo, Director of the Health Bacteriological Laboratory at Rome, on the Preservation of Viruses in Glycerine. In this paper, which is very short, the author does not do much more than just refer to the use of glycerine as an addition to vaccine lymph, and has obviously not altogether appreciated the importance of the results to be derived from such admixture. Indeed, he appears to mention it merely as an exception to a rule, which he considers fairly general, that many bacteria are preserved rather than destroyed by glycerine. As, however, he confirms in several particulars the results at which we have arrived, it will be well to briefly epitomise the paper in question.

"Glycerine is added nowadays in almost all vaccine institutions to vaccine emulsion, which by this means preserves its virulence for months, and even for years.

"As a proof of this I adduce the following*:—Dr. Krieger, after some experiments with calf lymph, overlooked a bottle of lymph in a press. He found it, and

* "Note sur le Vaccin de Genisse," par M. E. Deschamps, *Revue d'Hygiène*, N. S., p. 654.

used it *eleven* years afterwards, producing normal pustules and passing it through other subjects.

"The virus of rabies, too, remains unaltered in glycerine for a long time (Roux), and is active after six months (Ulfreduzzi).

"Further, many bacteria live well in glycerine, and they may be found preserved in glycerinated vaccine emulsion for various lengths of time. Their number, however, gradually diminishes, so that after some months' preservation the emulsion may retain its specific activity, but contain only a sparse number of living bacteria.

"I have extended my experiments in glycerine preservation to pathogenic bacteria found in the tissues of animals dead of infectious disease, using quite neutral unsterilized glycerine. I put spleens of such animals into 80-100 c.c. of glycerine, and kept them at the temperature of the room.

"Teased portions were subsequently inoculated subcutaneously in living animals. The bacteria used were the diplococcus of Fränkel, the bacillus of fowl cholera, and that of anthrax (? spore form)."

As the result of these experiments, Sclavo arrives at the following conclusions:—

The *diplococcus of Fränkel* preserves its virulence in glycerine for not less than sixty-seven days (also at forty-four and fifty-eight days).

Bacillus of fowl cholera—virulent after seventy-four days in glycerine, but killed by stay of four months.

With *anthrax*, virulence gradually decreased, ceasing in one experiment on the seventh and in another on the ninth day. At earlier periods incubation was prolonged in the living animal, and there was extensive subcutaneous œdema, while the bacteria showed a tendency to form long filaments in the blood, so that it may be that *the anthrax b. underwent a gradually increasing degree of attenuation in the glycerine.*

Of considerably greater importance from my point of view, however, is a paper by Chambon and Ménard which recently appeared.* In it these gentlemen relate their experience of the use of glycerinated vaccinal lymph when kept for a long time in capillary glass tubes previously sterilized and closed by the blow-pipe. The results they obtained with lymph originally good were highly satisfactory, and even lymph, which in its fresh state gave mediocre results, in

* *Gazette des Hôpitaux*, Dec. 15th, 1892.

the course of fifteen days produced a passable vesicle, and, after forty, fifty, or sixty days, a typical one. The improvement seemed due to the gradual extinction of parasitic microbes under the influence of glycerine and time.

Prof. Straus made plate cultures with their glycerinated lymph, which showed that when fresh it gave rise to numerous colonies of various microbes, especially staphylococcus pyogenes aureus and staphylococcus albus, while the glycerine lymph, fifty to sixty days old, remained absolutely sterile, intermediate specimens presenting fewer and fewer microbes as they became older. These experiments were repeated many times, and invariably with similar results.

This evidence, so entirely corroborative of my own work, is all the more important, as it appears certain, from a perusal of the original paper, that the authors were ignorant of the precisely similar results at which I had previously arrived, and which were published nearly twelve months before the appearance of their article.

There can thus, I venture to think, no longer be any doubt as to the superiority of the method of lymph storage which I advocate over the perhaps simpler method which has been so strenuously insisted on in England of late years, and I trust, therefore, that some authoritative pronouncement may before long be made on the matter, as it appears to me, at any rate, to be one which is of the utmost importance in relation to the present wide-spreading objection to vaccination on the score of the possible dangers incidental to the operation.*

No one, of course, denies that vaccination is liable to be complicated with erysipelatous, phagedænic, or pyæmic conditions; but all these latter undoubtedly are specific diseases due to specific causes, and when they arise in connection with cow-pox, whether in the cow or in man, are the results, not of the vaccine virus, but of specific poisons of a different kind, which have either been introduced with the vaccine virus or have inoculated the vaccinal sores at a later period.

It has, nevertheless, been frequently affirmed by some opponents of vaccination that erysipelas is an essential concomitant of vaccinia, and that given certain conditions —as, for instance, a lessened vitality in the child, or insani-

* From experiments which I have carried out, in part since this paper was read, it would appear that lanoline possesses the property of inhibiting the growth of saprophytic organisms in a similar manner to that exhibited by glycerine.

tary surroundings—it will gain the upper hand, causing injury and perhaps death, the ordinary manifestations of the vaccine virus itself either not appearing at all, or becoming aborted. Indeed, some go to the absurd length of considering the areola, which normally appears about the eighth day, as merely an indication of the presence of erysipelas in a more or less nascent condition.

Seeing that the streptococcus of erysipelas grows fairly readily, though it must be confessed somewhat capriciously, in ordinary nutrient media, it is obvious that, supposing no growth of any sort is obtained in a plate cultivation of glycerinated lymph of ascertained activity, the above-mentioned thesis cannot be sustained. In view, however, of the possible occurrence of the streptococcus in vaccine lymph, I thought it desirable to specially study the effect produced by the addition of glycerine to various nutrient media, which have been seeded from a pure cultivation of the streptococcus.

Such a cultivation I obtained through the kindness of Dr. Armand Ruffer. As, however, my experiments have not as yet been sufficiently exhaustive, I must defer details to a subsequent period, merely stating now that, in this case also, glycerine appears to inhibit the development of the streptococcus.

In conclusion, it may be well to briefly summarise the results at which I have arrived:—

1. The organisms to which the specific action of variolous and of vaccine lymph is due as yet are undiscovered.

2. Although this is the case, all the most reliable evidence, experimental and otherwise, is in favour of the organisms of these two diseases being identical in nature; the phenomena of vaccination being most probably due to an attenuation of the virus, caused in a similar manner to that witnessed in chicken cholera and other diseases, by sojourn in the tissues of an animal which is more or less refractory.

3. Monkeys react to inoculations of variola or vaccinia in a similar manner to the human being, and therefore afford a valuable means of controlling the results of experiments on the mutual relationship of these two diseases.

4. It is possible to isolate from vaccine (and also, to a less extent, from variolous) lymph a number of micro-organisms, none of which, however, have anything to do with the specific action of the lymph.

5. These bacteria belong in great part to that class which is concerned in the processes of suppuration, though

others, both pathogenic and non-pathogenic in nature, may be present also.

6. These "extraneous" bacteria may be destroyed if present, and in any case a guarantee of their absence may be afforded by the methods of treatment of the lymph which I have advocated.

7. By my method lymph may be preserved unimpaired for an indefinite period. Indeed, its specific activity, so far from being destroyed, may actually become intensified.

There now only remains the pleasant duty of expressing my sincere thanks to all those gentlemen who have aided me in my research. To Dr. Ricketts and Mr. Colclough, of the Hospital Ships, to Dr. Gornall, of the Warrington Small-pox Hospital, and to Dr. Berry, of the Monsal Fever Hospital, Manchester, I am indebted for supplies of variolous lymph; to Dr. Ruffer for a pure growth of the streptococcus of erysipelas; to Mr. Stanley Kent and Dr. Edmunds for photographs; and to Professor Foster, Mr. Power, Dr. Sherrington, Dr. Acland, and others, for much kindly help and criticism.

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